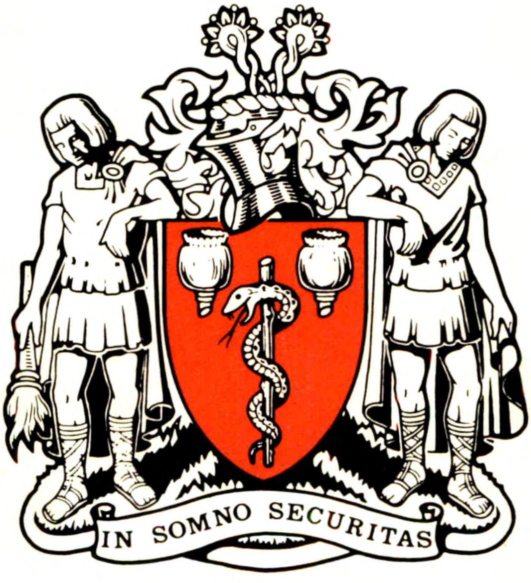
15.12.87
CUG-H02896-5-P02452

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 42 Number 9 September 1987

5

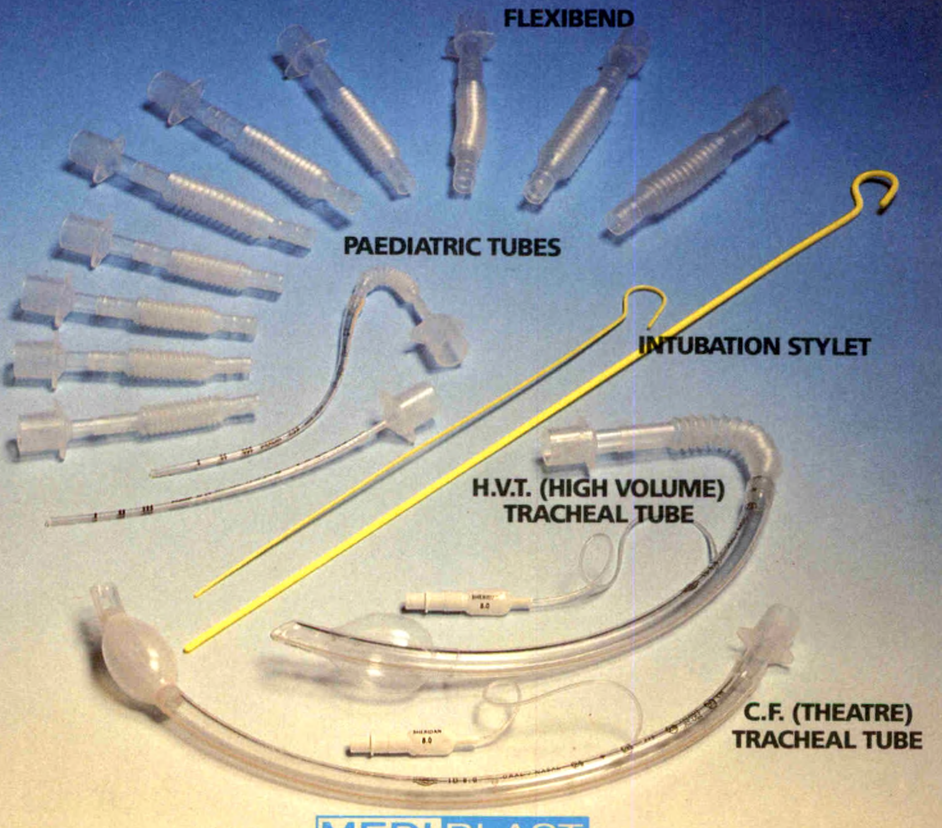


Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Austin
Boston Sydney Tokyo Toronto

ISSN 0003-2409

SEE US ON STAND 50 AT THE ANNUAL SCIENTIFIC MEETING

A NEW GENERATION OF INTUBATION


FLEXIBEND
PAEDIATRIC TUBES
INTUBATION STYLET
H.V.T. (HIGH VOLUME) TRACHEAL TUBE
C.F. (THEATRE) TRACHEAL TUBE

MEDIPLAST
PRESENT
THE SHERIDAN RANGE OF THEATRE, I. C. U. AND SPECIALITY ENDOTRACHEAL TUBES WITH UNIQUE FLEXIBEND CONNECTOR

For further information contact: Mediplast Ltd., 15 Fleming Close, Park Farm Industrial Estate, Wellingborough, Northamptonshire NN8 3UF Telephone: (0933) 675654 Telex: 311925 MEDPLA G

P, 24,522

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

---

Editor J. N. LUNN
Assistant Editors M. MORGAN, R. GREENBAUM, R. M. JONES, A. R. AITKENHEAD
Editor of *Anaesthesia News* J. N. HORTON
Editorial Board
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
Ex officio
The President of the Association M. ROSEN
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association P. MORRIS
The Immediate Past Honorary Secretary of the Association M. T. INMAN

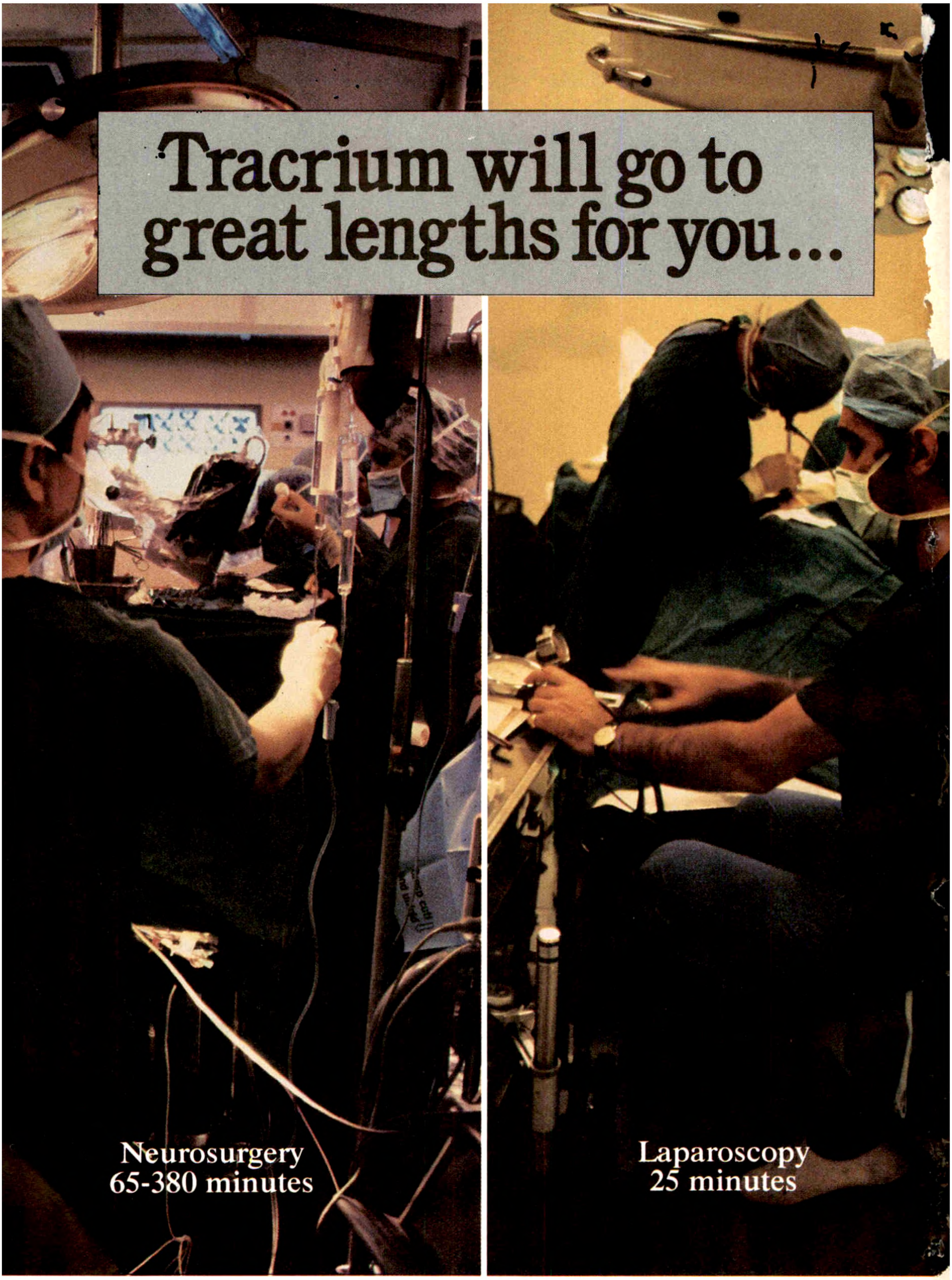
Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.

Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Limited for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
1987, Volume 42, 12 issues. Inland £90.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300–0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
U.S. POSTMASTER: send address changes to "Anaesthesia", c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Second class postage paid at Jamaica, New York 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
© 1987 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.
ISSN 0003-2409



ALMIC MEDICAL
DIVISION
HE WELLCOME FOUNDATION LTD

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

Tracrium Prescribing information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 month 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml are available.

Basic NHS costs £7.15 for a box of 5 x 2.5 ml ampoules. £13.75 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

1986
THE QUEEN'S AWARD FOR TECHNOLOGICAL ACHIEVEMENT TO THE WELLCOME RESEARCH LABORATORIES OF THE WELLCOME FOUNDATION LTD

TRACRIUM

Atracurium besylate

CALMIC MEDICAL
DIVISION

New Journal for 1987 . . .

JOURNAL OF CARDIOTHORACIC ANESTHESIA

Editor-in-Chief **Joel A. Kaplan**

Associate Editors

J. Earl Wynands, Cardiac Anesthesia
Roger Wilson, Thoracic Anesthesia
Dennis T. Mangano, Vascular Anesthesia

The Journal of Cardiothoracic Anesthesia is primarily aimed at anesthesiologists dealing with patients undergoing cardiac, thoracic, or vascular surgical procedures. In addition, a multidisciplinary approach will include contributions from cardiac, vascular, and thoracic surgeons, cardiologists, and other internists, intensivists, and related basic scientists. Emphasis will be placed on rapid publication of clinically relevant material applicable to the perioperative period. The purpose of the journal is to consolidate and disseminate original information in these important subspecialties of anesthesiology.

The Journal will publish editorials, original articles, brief clinical studies, large clinical series, case reports, invited state-of-the-art review articles, invited reviews of new drugs and equipment, controversial issues, pertinent abstracts from other journals, letters to the Editor, meeting summaries, news and notes, and book reviews. Innovative submissions using the latest techniques (e.g., two-dimensional color flow doppler and/or computer graphics) will be published at the Journal's expense. In addition, special supplement issues will highlight important topics. The Journal will be international in scope, with submissions encouraged from all continents. Every effort will be made to publish important new information in the shortest possible time. To further this goal of rapid publication in these constantly changing subspecialties, authors will be able to request an "expedited review" of their submissions. A positive "expedited review" will lead to rapid publication for new and controversial material.

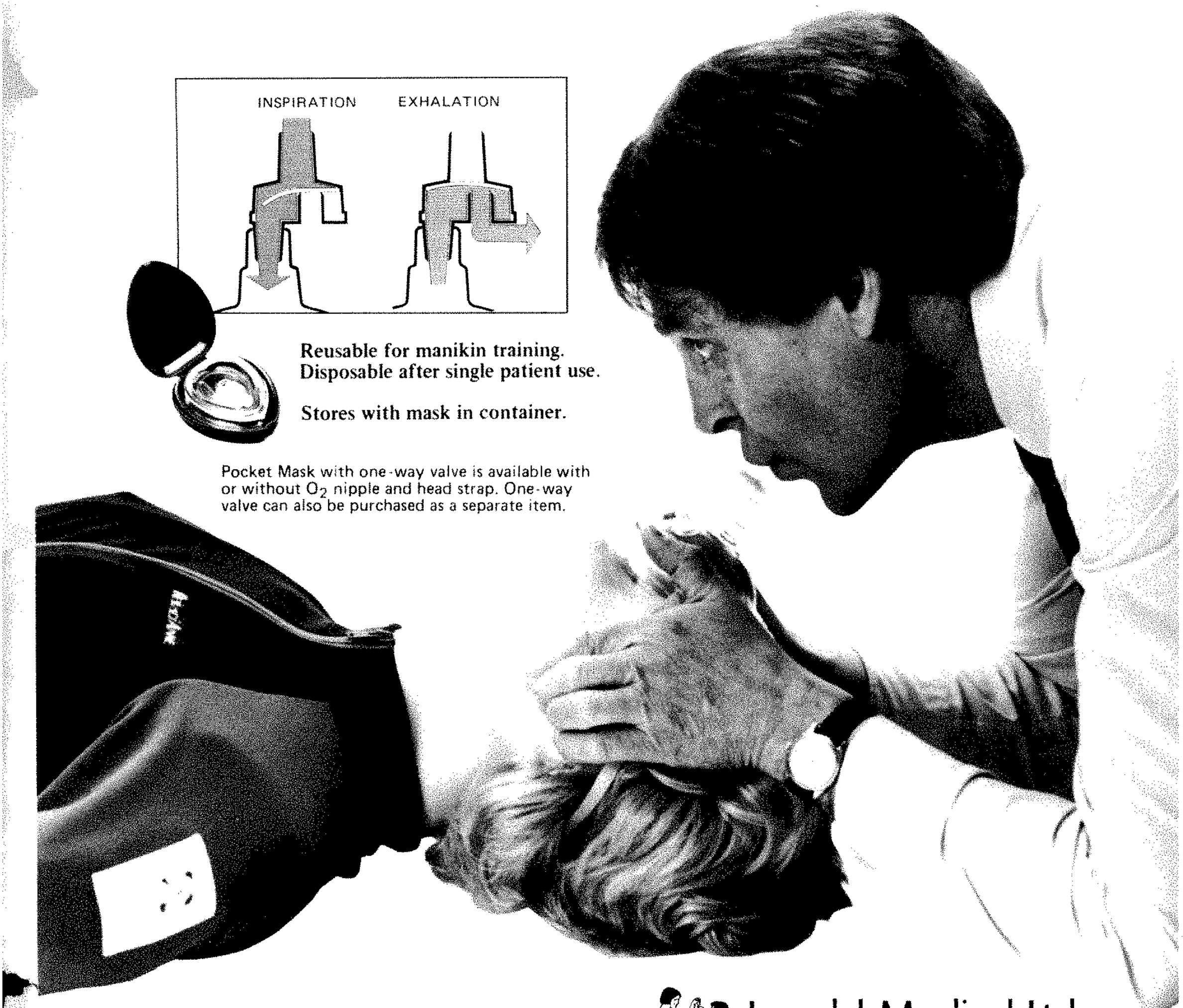
Publication: Bi-monthly
Subscription: Volume 1, 1987
Full Rate: $109.00 Overseas / £84.00 (U.K. Only)

For full subscription information and sample copies please apply to Journals Marketing Department at the addresses below.

Grune & Stratton

24–28 OVAL ROAD, LONDON NW1 7DX, UK
ORLANDO, FLORIDA 32887, USA

Laerdal Pocket Mask
with new One-Way Valve
Diverts patient's exhalation away from the rescuer



Reusable for manikin training.
Disposable after single patient use.

Stores with mask in container.

Pocket Mask with one-way valve is available with or without O_2 nipple and head strap. One-way valve can also be purchased as a separate item.

Laerdal Medical Ltd.
Laerdal House, Goodmead Road, Orpington, Kent BR6 OHX
Tel. Orpington (0689) 76634. Telex 8955251 LML G

UNIVERSITY OF BIRMINGHAM
DEPARTMENT OF ANAESTHETICS

QUEEN ELIZABETH HOSPITAL

in association with

JANSSEN PHARMACEUTICAL LTD

SYMPOSIUM ANNOUNCEMENT

"INFUSIONS IN ANAESTHESIA: THE CURRENT ART"

DATE: FRIDAY 20 NOVEMBER 1987
VENUE: BIRMINGHAM MEDICAL INSTITUTE

The Current Art for Infusing Narcotics, Hypnotics and Muscle Relaxants will be Discussed by:-

Professor D Stanski, California
Professor P Hutton, Birmingham
Professor C Hull, Newcastle upon Tyne
Professor G Jones, Leeds
Professor C Prys-Roberts, Bristol

Dr C Andrews, Plymouth
Dr J Bion, Birmingham
Dr D Coates, Bristol
Dr B Fischer, Bromsgrove
Dr J Viby Morgensen, Copenhagen
Dr J Sear, Oxford

FOR FURTHER INFORMATION, PLEASE CONTACT
MISS JUDITH ALEXANDER, CONFERENCE COORDINATOR, JANSSEN PHARMACEUTICAL LTD,
GROVE, WANTAGE, OXON OX12 0DQ. TELEPHONE (02357) 2966

Association of Anaesthetists
of Great Britain and Ireland,
9 Bedford Square,
London WC1B 3RA

Tel: 01 631 1650

Faculty of Anaesthetists,
Royal College of Surgeons,
35/43 Lincoln's Inn Fields,
London WC2A 3PN

Tel: 01 405 3474

Postgraduate Study Day

Saturday, 17th October 1987
9.30am–4.45pm

at
THE ROYAL COLLEGE OF SURGEONS
LINCOLN'S INN FIELDS, LONDON WC2A 3PN

The Postgraduate Study Day is jointly sponsored by the Association of Anaesthetists and the Faculty of Anaesthetists. All anaesthetists are eligible to attend. The programme will consist of 18 lectures, in three different rooms, enabling participants to attend their choice of six lectures in the course of the day.

Application forms may be obtained from the Association of Anaesthetists (Tel.: 01–631 1650). Registration fee £30, excluding lunch.

Wiley

CHICHESTER · NEW YORK
BRISBANE · TORONTO · SINGAPORE

Current European Anaesthesiology
Volume 3 1987
The Yearbook of the Academy of Anaesthesiology

Volume 3 of the European Academy of Anaesthesiology's Yearbook covers a wide range of important new developments in anaesthesiology which have emerged in Europe in recent years.
As before the book presents a wide variety of topics giving a broad view of current research and practice. Summaries of papers published in relevant European journals are presented, and each is reviewed by an expert in the subject who evaluates the paper's clinical significance and its applicability to contemporary practice.
The yearbook is a unique source of information for students, researchers and practitioners, who will find it a valuable reference point on many different aspects of the subject not available elsewhere in such accessible form.

047191682X approx 325pp September 1987
approx £30.00/$59.40

Also available:

Volume One
0471907103 320pp 1985 £29.50/$55.20
Volume Two
0471911127 330pp 1986 £29.50/$55.20

Problems in Obstetric Anaesthesia

Guest Editor: BARBARA MORGAN, Department of Anaesthetics, Queen Charlotte's Maternity Hospital, London, UK

The use of obstetric anaesthesia in obstetrics is a subject of major significance to obstetricians and paediatricians, as well as anaesthetists. This book discusses the problems and complications which can arise during pregnancy and labour such as aspiration of gastric contents, massive blood loss, intravascular coagulation etc., and also presents the latest information on treatment of shock, complications of epidural anaesthesia, and the fetal and neonatel effects of analgesic and anaesthetic drugs.

"It is excellently produced and should be recommended reading for all concerned in the care of women in labour"
British Medical Journal

Volume 3 in the Perinatal Practice Series.

0471909572 210pp 1987 £32.50/$60.80

Wiley books are available through your bookseller. Alternatively, order direct from Wiley (payment to John Wiley & Sons Ltd). Credit card orders accepted by telephone — (0243) 829121 or FREEFONE 3477.

JOHN WILEY & SONS LTD
BAFFINS LANE · CHICHESTER · W. SUSSEX PO19 1UD

VYGON

Many speak of Seldinger but . . .

VYGON
124
leader cath
Made in France
Cathéter intravasculaire ORX avec guide métallique (méthode de Seldinger) pour la voie sous-clavière
XRO intravascular catheter with metal spring guide (Seldinger-method) for subclavian introduction
VYGON

Seldinger speaks only of Leader-Cath

Sven-Ivar Seldinger

Vygon (UK) Limited, Bridge Road,
CIRENCESTER, Glos., GL7 1PT.
Telephone: (0285) 67051 Telex: 43342 VYGON G

"Please send me details of the Leader-Cath range"

Name:
Designation:
Hospital: Ext:
Address:
Telephone:

ANAESTHESIA HAS COME A

POST op CARE

[illegible]

ONG WAY...

...SO HAS REVERSAL

In recent years, many advances have been made in the fiel of anaesthesia, including reversal of residual neuromuscula blockade.

A. H. Robins has been a major contributor to this are with Robinul, an anticholinergic agent which provides significant advantages over atropine.

Robinul produces less initial tachycardia, and bette protection against the peripheral muscarinic effects of neostigmine than atropine. In addition, the quality of recover after Robinul is better than after atropine, due to limite penetration of Robinul into the central nervous system.

Clinical experience has demonstrated that simultaneous administration of Robinul and neostigmine is associate with greater cardiostability at reversal, than separate injections. This had led A. H. Robins to develop ROBINUL NEOSTIGMINE injection, a ready prepared mixture containing standard doses of Robinul and neostigmine for reversa in a 1ml ampoule.

Robinul-neostigmine injection provides dependabl and convenient reversal of residual neuromuscular blockade contributing further towards improvements in anaesthesia.

diac dysrhythmias, hypertension, thyrotoxicosis, epilepsy or Parkinsonism. e with caution in patients with intestinal anastomoses. Safety in pregnancy/ tation has not been established. **Basic NHS price** £9.40 (10 x 1ml ampoules). **gal Category** POM **Package Quantities** Packs of 10 ampoules. **Further ormation** Robinul Neostigmine Injection can be used when atropine has been ed as a pre-operative anti-cholinergic. **Product Licence Number** 0100/0099. **oduct Authorisation Number** 86/27/1

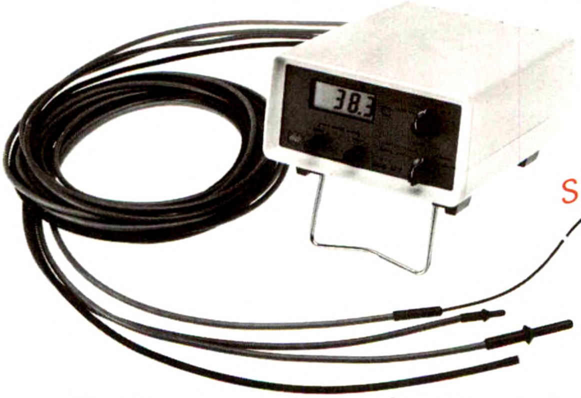
ROBINUL®

GLYCOPYRROLATE

NEOSTIGMINE

Temperature Monitoring

- 40 years experience
- Quality & Reliability
- Sales in 120 countries



SEE US AT
THE ANNUAL
SCIENTIFIC MEETING
SHEFFIELD

9th - 11th
SEPTEMBER

40 years experience is your guarantee for precision temperature measurements.

For information on our instruments and comprehensive list of probes, contact:—

ELLAB UK LTD

15 Church Crofts, Castle Rising, King's Lynn, Norfolk PE31 6BG
Tel: Castle Rising (055387) 611

A Division of ELLAB A/S. Krondalvej 9. DK-2610 Rødovre, Denmark.
Telephone: 45 2 949211. Telex: 35311 ellab dk.

ellab INSTRUMENTS

Hespan*

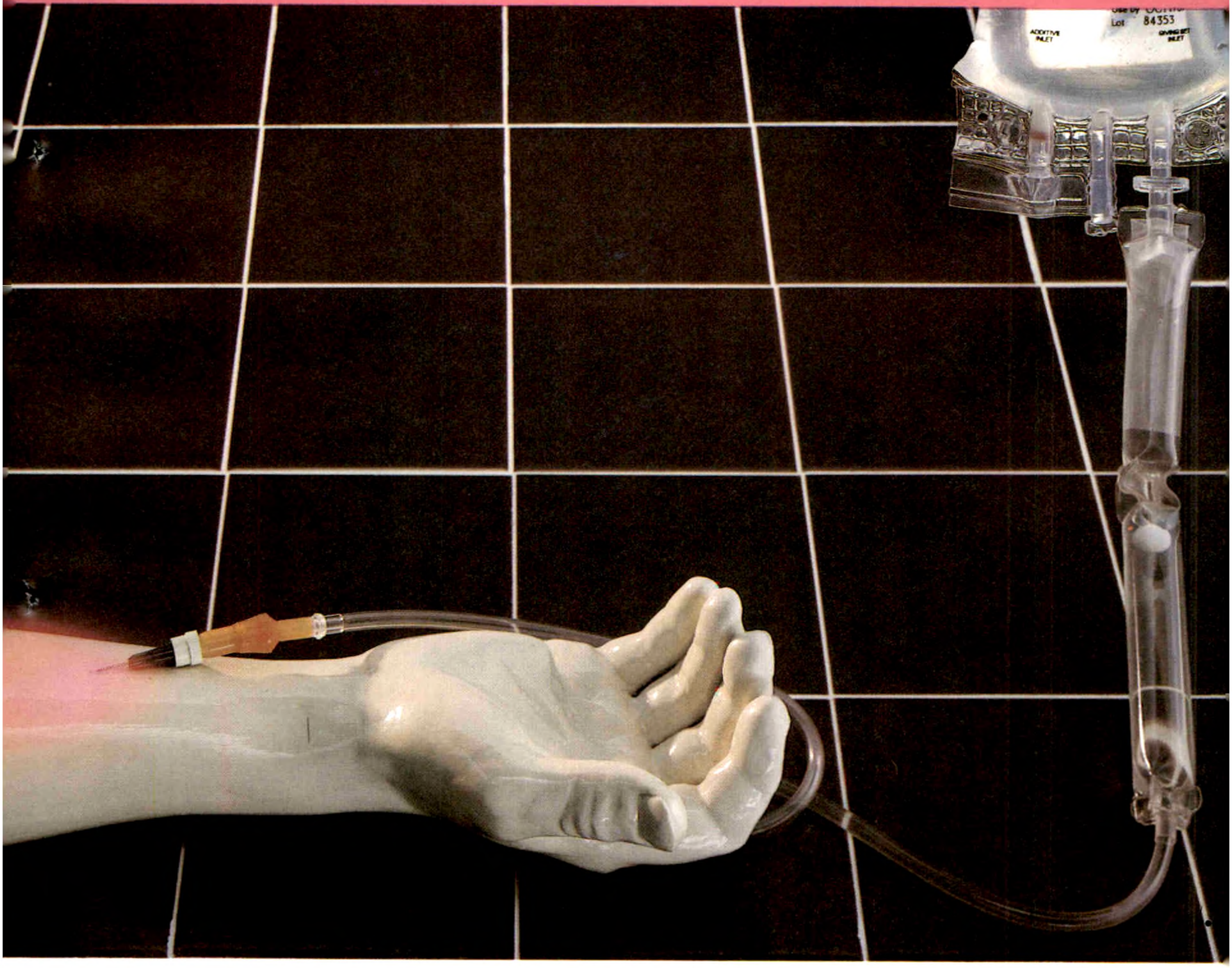
Hetastarch 6%

Controls plasma volume for a full 24 hours

Rapid plasma volume expansion restores cardiac output and tissue perfusion for vital organ function.[1-3]

Reliable increase in colloid osmotic pressure reduces the risk of tissue and pulmonary oedema.[4]

Available freely without dependence on blood donations, without the risk of transmitting disease.



References 1. S. Lazrove, *et al., Crit. Care Med.*, 1980, *8(5).* **2.** V.K. Puri, *et al.* Data on file. **3.** V. Hempel, *et al., Anaesthetist*, 1975, *24*, 198-201. **4.** M.T. Haupt and E.C. Rackow, *Crit. Care Med.*, 1982, *10*, 159-162. For full prescribing information see next page. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel: (0438) 734549.

DU PONT

*Registered trademark

Hespan Prescribing Information

Composition Each 100ml Hespan contains: Hetastarch 6.0g. Sodium Chloride BP 0.9g. Water for Injections BP qs, pH adjusted with Sodium Hydroxide. **Indications** 1. As a plasma volume expander in hypovolaemia. 2. Leucapheresis. 3. Extracorporeal circulation. **Contraindications Warnings** There are no absolute contraindications to the use of Hespan. Use with caution in patients with established renal failure. Hespan can produce dilutional effects on fibrinogen and prothrombin activity. In large volumes, Hespan may alter the coagulation mechanism and produce a transient prolongation of the clotting time. Use with caution in patients with severe bleeding disorders. Use with caution in patients vulnerable to vascular overloading. Caution should be observed before administering Hespan to patients with a history of liver disease in view of slightly raised indirect bilirubin levels observed on very rare occasions in volunteers. There is a low incidence of allergic reactions and the administration is not associated with raised plasma histamine levels. Mild periorbital oedema, urticaria or wheezing have been reported and are readily controlled by discontinuation of the drug and, if necessary, administration of an antihistamine. **Dosage and Administration—Plasma Volume Expansion** Intravenous infusion only, in an initial volume approximately equal to half the estimated blood loss. In adults the amount usually administered is 500ml to 1,000ml. Total dosage does not usually exceed 1,500ml per day or 20ml per kg of bodyweight for a typical 70kg patient, however the limiting dose will depend on circulating volume and haematocrit. In acute haemorrhagic shock, an initial administration rate approximately 20ml/kg/hr may be recommended, in burns or septic shock, it is usually administered at slower rates. **Leucapheresis** 250-700ml Hespan is typically added to the Y junction just above the bleed out in the ratio of 1 part citrated Hespan to at least 8 parts whole blood, ratios of 1:20 have been used. On rare occasions, 500ml Hespan has been infused into the donors 15-30 minutes before collection. Multiple leucapheresis procedures using Hespan of up to 2 per week or a total of 7-10 have been reported to be safe and effective. The safety of more frequent or a greater number of procedures has not yet been established. **Product Licence Number** 2737/0042. **Package Quantities** Hespan is supplied in 500ml flexible plastic bags. Basic price £16.72. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel. (0438) 734549.

DUPONT

ANESTHESIA AND THE GERIATRIC PATIENT

Edited by
SUSAN WILSON KRECHEL, M.D.

Anesthesia and the Geriatric Patient represents the state of the art in the long-neglected area of anesthetic management of elderly patients. This new book features a collection of the most pertinent and informative topics on the subject. Approximately one-third of the book is devoted to basic science topics on physiology and pharmacology of aging as related to anesthesia practice with the remainder focusing on clinical aspects.

1984, 272pp., $44.50/£37.50
ISBN: 0.8089.1661.0

CLINICAL FEATURES IN ANESTHESIOLOGY

Edited by
JONATHAN L. BENUMOF,
University of California,
San Diego School of Medicine.

A Volume in the ANESTHESIA UPDATE Series

Covering the entire scope of anesthesia from both clinical and basic science perspectives, this comprehensive work presents the latest important developments in anesthesiology. With a concise emphasis on what is really "new" in the field, individual chapters by well-known experts discuss such vital issues as: • recent developments and breakthroughs in pharmocology • anesthesia techniques in operative, pre- and postoperative environments • special topics in the evolution of anesthesia, including a history of anesthesia and future directions • drug abuse in the medical profession.

1983, 288pp., $39.50/£33.00
ISBN: 0.8089.1580.0

Grune and Stratton

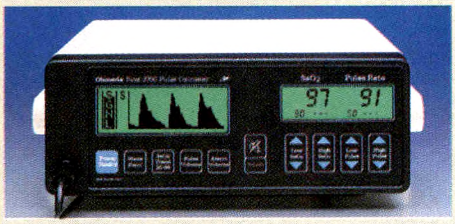
ORLANDO, FLORIDA 32887, U.S.A.
24-28 Oval Road, London NW1 7DX,
England

Now there's a whole new way to look at pulse oximetry.

Representational not

Ohmeda announces a bright new display.

The Ohmeda Biox 3700 has a bright new LCD that you can really read, three times brighter than before. The panel is easy to see, whether you are standing or sitting, from as far away as 20 feet.



Plus the perfect probe.

The high intensity light source of the new Flex II probe provides a steady, strong signal, able to penetrate variable tissue thickness or pigmentation. Its softer material allows fast, easy application on multiple patient sites. Plus, the economical Flex II is *re-usable* and more flexible, perfect for neonatal and pediatric patients.

Only from Ohmeda—the Company that listens when you talk pulse oximetry.

We're proud to be the original innovators in pulse oximetry. We've been with you from the start—in the OR and in the ICU, in the lab, on your rounds, and in the field for home care. Ohmeda has listened to your ideas and responded to your needs with the exciting new bright display and the revolutionary Flex II *re-usable* probe. And our new software makes the 3700 easy to use on low perfusion patients and during sleep studies. Proof that Ohmeda puts your best and brightest ideas to work, exactly as you envisioned them.

A new display. A new probe. Both ready for you now.

Your Ohmeda representative has the new 3700 and Flex II re-usable probe ready for delivery. Call us today for your complimentary demonstration. With our field sales and service organization located throughout the world, you'll be looking on the bright side of pulse oximetry right away.

Ohmeda

Ohmeda
Elizabeth Way
Harlow, Essex CM 19 5AB
U.K. Sales Telephone 0279 442001
Telex 81497 OHMEDH G
A Division of The BOC Group Inc.
BOC Health Care

Form #E001 © 1987 The BOC Group Inc

Anaesthesia with security

Prescribing Information: FORANE® (isoflurane) **Indications:** for inhalation anaesthesia. **Dose:** induction should begin at 0.5% and be adjusted appropriately. Maintenance concentrations generally lie between 1.0% and 2.5%. Elderly: lesser concentrations normally required. Children: adequate data are not available in children under two years of age. **Contraindications:** know sensitivity to Forane, or a history of malignant hyperthermia following a previous adminstration. **Side-effects:** hypotension and respiratory depression. Shivering, nausea and vomiting may occur during recovery. **Basic N.H.S. price:** £33.50 per 100ml. **P.L. Number:** 0037/0115.

Abbott Laboratories Limited
Queenborough, Kent ME11 5EL

Anaesthesia, 1987, Volume 42, page 927–928

Editorial

Down the tube

The administration of medicines by the inhalational route is undoubtedly as old as medicine. The delivery of potent and effective drugs by this route probably began with the discovery of anaesthesia. In 1912 Ephraim[1] recommended adrenaline by inhalation for the treatment of asthmatic attacks. He noted that bronchial application caused blanching of the mucous membranes and recommended tracheal application of a nebulised aerosol. However, the method fell into disuse because of difficulties of dose control and successful dispersal to the bronchioles. Nevertheless, there were occasional reports of the efficacy of nebulised adrenaline.[2] The effects of adrenaline were thought to be local and restriction of the total dose would avoid systemic toxicity.

The factors which affect the retention of aerosol particles have been intensely studied since the 1960s. Aerosols can be defined as liquid or solid particles which are so small that they remain suspended in air rather than sediment quickly under the influence of gravity. The studies of Hatch and Gross[3] in 1964 demonstrated that larger particles never reach the distal airways. Particles over 100 micrometres are completely removed in the upper airway and do not reach the alveolar sacs, 5 micrometres are half removed and 2 micrometres are one-fifth removed. There is little particle removal in the upper airway of particles of less than 5 micrometres and the alveoli provide a large surface area for drug absorption.[3]

Swann and Spafford[4] demonstrated that fluid is rapidly absorbed from the lungs in drowning and Redding[5] compared intramuscular, intravenous, intracardiac and tracheal adrenaline in the resuscitation of dogs. He found that tracheal adrenaline diluted in 10 ml water or saline was comparable to intracardiac adrenaline in effect and it is clearly a simpler and safer method of adrenaline administration.

Most subsequent studies of the tracheal route of drug administration have been performed on non-arrested dogs, although a few have studied hypotensive animals or animals with cardiac arrest.[6,7] Quinton and his colleagues[8] recently compared the use of 10 ml tracheal adrenaline 1:10 000 with 1 ml adrenaline 1:1000 given intravenously to twelve patients who presented in the accident and emergency department with asystolic cardiac arrest. The tracheal route produced no change in serum adrenaline and no clinical response.

Digitalis, diuretics, tranquillisers, penicillin, atropine and adrenaline have been administered as aerosols and the tracheal route has the endorsement of the American Heart Association[9] and the Resuscitation Council in the United Kingdom,[10] but little is known about the optimal drug dosage, volume of solution, pH and fundamental pharmacokinetics. Adrenaline was given in up to ten times greater dosage than that required by the intravenous route, although in the baboon, the same dose as intravenously seems to be efficacious.[11] Greenberg[12] found that instillation of water into the trachea (2 ml/kg) led to a marked decrease in arterial oxygen tension and therefore suggested that drugs for the tracheal route should be dissolved in saline.

The study by Bray and her colleagues to appear in the November issue demonstrates the rapid onset and efficacious action of tracheal atropine. These authors used 0.6 mg atropine in 1 ml solution, although Greenberg's group suggested 1 mg as a minimum adult tracheal dose but did not specify the volume of solution used in their case report.[13] Redding's original study[5] found 10 ml better than 1 ml of solution and most studies suggest 5–10 ml is the appropriate volume.

Drugs currently used include adrenaline, lignocaine, naloxone and diazepam. Calcium, strong bicarbonate or other known irritant or hyperosmolar solutions are contraindicated. The technique of tracheal drug therapy must be meticulous. A fine bore catheter should be inserted to the tip of the tracheal tube and, immediately after instillation of the drug, a few manual hyperinflations should be

0003–2409/87/090927 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

performed to disseminate the drug bilaterally and distally.[14] Tracheal administration of emergency drugs is very easy but may be unreliable in the event of cardiac arrest; it can facilitate the entry of foreign bodies into the trachea and fuller clinical and scientific evaluation is still awaited.

University College Hospital,
London WCIE 6AU

R. GREENBAUM
Assistant Editor

References

1. EPHRAIM A. Uber des Wirkung des Adrenalins beim Asthma bronchiale und bei der chronischen Bronchitis. *Deutsche Medizinische Wochenschrift* 1912; **38:** 1453.
2. NIELSEN NA. Treatment of asthmatic attacks by inhalation of adrenaline. *Lancet* 1936; **2:** 848–9.
3. HATCH TH, GROSS P. *Pulmonary deposition and retention of inhaled aerosols.* New York: Academic Press, 1964.
4. SWANN HG, SPAFFORD NR. Body salt and water changes during fresh and sea water drowning. *Texas Reports on Biology and Medicine* 1951; **9:** 356–82.
5. REDDING JS, ASUNCION JS, PEARSON JW. Effective routes for drug administration during cardiac arrest. *Anesthesia and Analgesia* 1967; **46:** 253–8.
6. ELAM J. The intrapulmonary route for CPR drugs. In: SAFER P, ed. *Advances in cardiopulmonary resuscitation.* New York: Springer-Verlag, 1977: 132–40.
7. RALSTON SH, VOORHEES WD, BABBS CF. Intrapulmonary epinephrine during prolonged cardiopulmonary resuscitation: improved regional blood flow and resuscitation in dogs. *Annals of Emergency Medicine* 1984; **13:** 79–86.
8. QUINTON DN, O'BYRNE G, AITKENHEAD AR. Comparison of endotracheal and peripheral intravenous adrenaline in cardiac arrest. Is the endotracheal route reliable? *Lancet* 1987; **1:** 828–9.
9. AMERICAN HEART ASSOCIATION. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). Parts 3 and 4. *Journal of the American Medical Association* 1986; **255:** 2933–69.
10. RESUSCITATION COUNCIL (UNITED KINGDOM). *Resuscitation for the citizen.* Department of Anaesthetics, The Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS: The Resuscitation Council (UK), 1984.
11. CHERNOW B, HOLBROOK P, D'ANGONA DS, ZARITSKY A, CASEY LC, FLETCHER JR, LAKE CR. Epinephrine absorption after intratracheal administration. *Anesthesia and Analgesia* 1987; **63:** 829–32.
12. GREENBERG MI, BASKIN SI, KAPLAN AM, URRICHIO FJ. Effects of endotracheally administered distilled water and normal saline on the arterial blood gases of dogs. *Annals of Emergency Medicine* 1982; **11:** 600–4.
13. GREENBERG MI, MAYEDA DV, CHRZANOWSKI R, BRUMWELL D, BASKIN SI, ROBERTS JR. Endotracheal administration of atropine sulfate. *Annals of Emergency Medicine* 1982; **11:** 546–8.
14. GREENBERG MI, SPIVEY WH. Comparison of deep and shallow endotracheal administration of dionosil in dogs and effect of manual hyperventilation. *Annals of Emergency Medicine* 1985; **14:** 209–12.

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 3 months of receipt.

Anaesthesia, 1987, Volume 42, pages 929–937

Propofol infusion for sedation in intensive care

L. H. NEWMAN, J. C. McDONALD, P. G. M. WALLACE AND
I. McA. LEDINGHAM

Summary

Ten patients, with a range of illness severity, received a continuous 8-hour infusion of undiluted propofol for sedation while undergoing mechanical ventilation in a general intensive care unit. The level of sedation was assessed hourly and measurements were made of haemodynamic, respiratory, haematological and biochemical variables. Sedation remained satisfactory in most patients throughout the study period, with only occasional alterations in infusion rate, and eight patients required further sedative therapy within 45 minutes of discontinuation of the propofol infusion. Arterial pressure tended to decrease from baseline values; mean and diastolic pressures demonstrated a significant decrease ($p < 0.05$) at 4, 7 and 8 hours during the infusion. Adrenal steroidogenesis was not inhibited significantly.

Propofol infusion proved to be a useful and readily controllable sedative agent, and discontinuation of the drug was followed by rapid recovery in most cases. The critically ill may be particularly sensitive to the cardiovascular depressant properties of the drug.

Key words

Anaesthetics, intravenous; propofol.
Intensive care; sedation.

Sedation is frequently used in intensive care units to allay patient anxiety and to relieve the discomfort associated with procedures such as mechanical ventilation, physiotherapy and insertion of monitoring lines. A wide range of drugs has been used for these purposes. At present, an opiate–benzodiazepine combination is most commonly employed.[1]

Prolonged continuous intravenous infusions of certain anaesthetic induction agents were favoured in some centres[2,3] but their use has declined since the withdrawal of Althesin and etomidate in 1984. Althesin was found to activate complement, an action attributable to its solubilising agent, Cremophor EL, with the risk of serious anaphylactoid reactions. In the case of etomidate, work from this centre[4] revealed a marked increase in mortality amongst multiple trauma patients who received long-term infusion, and later experimental studies showed the agent to be a potent inhibitor of adrenocortical function.[5,6]

Propofol (2,6-di-isopropylphenol) is an alkylphenol which has been widely investigated for use as an anaesthetic induction agent. It was initially formulated in Cremophor EL but it has

---

L.H. Newman, MB, ChB, FFARCS, J.C. McDonald, MB, ChB, FFARCS, Registrars, Clinical Shock Study Group, P.G.M. Wallace, MB, ChB, FFARCS, Consultant, Intensive Care Unit, I.McA. Ledingham, MD, FRCS, FRCP, FRSE, Professor of Intensive Care, Western Infirmary, Glasgow G11 6NT.

0003–2409/87/090929 + 09 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

more recently been prepared as an aqueous soya bean emulsion formulation, which has been demonstrated in animals to be unlikely to produce anaphylactoid reactions.[7] Propofol is metabolised rapidly and is, in theory, a suitable agent for infusion techniques.

We have performed a clinical trial that investigates the use of propofol by infusion for sedation in general intensive care patients who require mechanical ventilation.

Methods

Hospital ethical committee approval was obtained. Ten patients, aged between 56 and 77 years, admitted to the intensive care unit and who required mechanical ventilation for a period expected to exceed 8 hours' duration, were selected for the study. Patients with head injury, possible pregnancy or previous adverse reactions to general anaesthesia were excluded. Informed consent was obtained from next of kin in all cases.

When sedation was required before consent was obtained, patients were given bolus doses of morphine and/or midazolam as used routinely in this unit. After consent had been obtained, and when the normal indications for sedation were established, clinical and laboratory assessments were performed prior to the start of the study. Electrocardiogram, intra-arterial pressure and central venous pressure were monitored routinely in all cases.

Initial clinical assessment included heart rate, systolic and diastolic arterial pressures, central venous pressure, airway pressure, core and peripheral temperatures and an assessment of initial level of sedation; baseline laboratory assessment included arterial blood gases, full blood count, platelets, prothrombin time, urea, creatinine and electrolytes, liver function tests, ACTH and plasma cortisol. Blood gas results were used to calculate the alveolar–arterial oxygen tension gradient ($(A - a)Do_2$).

If clinically indicated by the initial level of sedation, a pre-infusion bolus of propofol 1 mg/kg, based on measured or estimated weight, was given. Otherwise, an infusion of propofol was administered at a rate of 1.15–3 mg/kg/hour (as an undiluted 1% aqueous emulsion containing propofol 10 mg/ml) by an infusion pump through a central vein.

The desired level of sedation was judged to be that at which the patient remained comfortable without periods of agitation, asleep while undisturbed, yet rousable with relative ease in response to the spoken word, tracheal suction or painful stimuli. The infusion rate of propofol was adjusted to achieve this desired level whenever possible; any alterations in dosage were noted.

The infusion was continued for a period of 8 hours, during which further clinical and laboratory assessments were performed. Clinical assessments as previously listed, together with arterial blood gases, were repeated at hourly intervals throughout the duration of the infusion. An arterial blood sample was withdrawn 4 hours after the infusion was started, for estimation of ACTH and plasma cortisol. At 8 hours, all laboratory assessments were repeated and the infusion discontinued. Thirty minutes later each patient received Synacthen 250 μg intramuscularly; blood samples were withdrawn for estimation of plasma cortisol 30 and 120 minutes later.

A sample of blood was inspected for the presence of lipaemia at the start of the infusion period and at 4 and 8 hours. All laboratory assessments, with the exception of arterial blood gases, ACTH and plasma cortisol, were repeated 24 hours after baseline samples were taken.

Before the infusion was started and at hourly intervals, 2.5-ml samples of blood were withdrawn into tubes containing potassium oxalate and stored at 4°C until transfer to ICI Pharmaceuticals for estimation of blood propofol levels.

The level of sedation was assessed hourly throughout the infusion period. This was achieved by the use of a linear analogue scale for determination of a consciousness score (0, complete unrousability; 10, fully awake and receptive), together with a subjective assessment of agitation when roused. Patients were initially observed while undisturbed and then stimuli of varying intensity were applied to achieve arousal. Stimuli were graded from the spoken word to tracheal suction and painful stimuli. The patient was assigned a point on the linear analogue scale according to ease of rousability, and this determined the consciousness score. If a patient was unacceptably agitated on arousal, this was considered to represent inadequate sedation and the infusion rate was increased accordingly, while the infusion rate was decreased if arousal proved difficult. All assess-

Table 1. Patient details.

Patient	Sex	Age (years)	Weight (kg)	APACHE II worst score in first 24 hours	Diagnosis
1	F	71	36	10	Postoperative laryngopharyngo-oesophagectomy
2	M	59	58	12	Acute exacerbation COAD, respiratory failure
3	F	56	50	12	Acute exacerbation COAD, respiratory failure
4	M	69	65	15	ARDS 2 weeks postoperatively
5	M	58	62	11	Postoperative oesophagogastrectomy
6	M	69	80	18	Postoperative repair of chest stab wound
7	M	58	67	3	Postoperative infected aortic graft
8	M	69	85	10	Postoperative aortic graft
9	F	58	45	21	Postoperative bowel surgery, septic shock
10	F	77	69	16	Postoperative bowel surgery, poor respiratory function

COAD, Chronic obstructive airways disease; ARDS, adult respiratory distress syndrome.

ments were made throughout the period of study on each patient by one of two observers (L.H.N. and J.C.M.); supervision of level of sedation and infusion rate was virtually continuous.

Patients were ventilated mechanically at normocapnia with oxygen-enriched air. Muscle relaxants were avoided whenever possible, as consistent with the policy of this unit, and other treatments such as blood transfusion, antibiotics, inotropic agents and diuretics, were administered as required. Propofol infusion was supplemented as necessary by morphine boluses if the patient, or his clinical condition, indicated the presence of pain. Intravenous fluids were administered as necessary to maintain an adequate central venous pressure. Following discontinuation of propofol, the usual sedative regimen used on the unit was made available and the time of first requirement for sedation noted.

APACHE II scores,[8] using worst values within the first 24 hours of admission, were calculated for each patient in order to compare severity of illness. Blood and intravenous fluid requirements and urine output over the period of infusion were recorded. Any side effects attributable to propofol were carefully documented.

Laboratory analyses were performed using standard techniques. Plasma cortisol and ACTH concentrations were measured by radioimmunoassay. The reference range for plasma cortisol was 110–770 nmol/litre, depending upon time of blood sampling.

Student's *t*-test (paired) was applied for statistical analysis of measurements of arterial pressures, heart rate, central venous pressure, airway pressure, blood gases, $(A - a)D_{O_2}$ and plasma cortisol. The Wilcoxon signed rank test was applied to haematological and clinical chemistry data.

Results

All ten patients completed the 8-hour study period. Clinical details of the patients are shown in Table 1. All but one of the admission APACHE II scores exceeded 10; this indicates that the majority of patients were moderately to severely ill.

Sedation

Three patients received a bolus dose of propofol 1 mg/kg prior to the start of infusion. The mean total dose of propofol administered was 978 mg (range 570–1990 mg) and the mean infusion rate throughout the study was 1.93 mg/kg/hour (range 1.03–2.81 mg/kg/hour).

Variation existed in the acceptable level of sedation which individual patients required to remain comfortable and free from agitation. Table 2 shows the consciousness scores, together with blood propofol levels, at each of the hourly assessments during the infusion period. Several patients had blood propofol estimations at 60 and 150 minutes after the infusion was stopped, and mean values at these times are also shown.

The infusion rate was changed an average of four times (range 2–8) during the 8-hour period, as indicated by individual adequacy of sedation. The time to next sedative requirement was used as an assessment of recovery time. Eight of the 10 patients recovered consciousness to a degree which required further sedation, either because of agitation or inability to comply with mechani-

Table 2. Consciousness scores and blood propofol levels during study.

	Time from start of infusion (hours)										
	0	1	2	3	4	5	6	7	8	9 ($n = 9$)	10.5 ($n = 6$)
Consciousness score											
Mean	4.4	2.6	3.1	3.3	3.6	3.1	2.8	2.9	3.1		
Range	0.9–7.4	0–6.8	2.2–5.2	0.8–5.0	1.9–5.4	0.6–5.8	1.4–5.8	1.0–6.2	0.9–5.8		
Blood propofol level, μg/ml											
Mean	0	0.71	0.63	0.74	0.67	0.92	0.95	0.83	0.88	0.27	0.17
Range	—	0.31–1.69	0.16–1.46	<0.14–1.55	0.21–1.37	0.31–1.37	0.56–1.92	0.49–1.55	0.55–1.59	0.11–0.44	<0.09–0.34

cal ventilation, within 45 minutes after the propofol infusion was stopped. Of these eight patients, one was sufficiently alert to be considered suitable, after respiratory assessment, for spontaneous ventilation and extubation 22 minutes after discontinuation of propofol.

Four patients received boluses of morphine either for painful procedures or because of evidence of pain during the period of sedation with propofol. Another patient had previously experienced frequent anginal attacks and received glyceryl trinitrate and morphine (2 mg/hour) by infusion throughout the 8-hour study period. This patient required the lowest mean propofol infusion rate to maintain sedation (1.03 mg/kg/hour). One further patient required additional sedation because of agitation and received a single bolus of midazolam. Four of the 10 patients required no supplements to the propofol infusion.

The initial level of sedation on entry to the study was variable because some patients were admitted directly from theatre and had recently received muscle relaxants. Propofol infusion was started in the presence of partial paralysis if necessary. However, no patient required muscle relaxants to facilitate ventilation during the study period.

Cardiovascular variables

Of the three patients who received a bolus of propofol prior to the infusion, two exhibited marked decreases in mean arterial pressure of 40% and 53%. Patients 5 and 8 were hypertensive on admission to the study and received either hydralazine or labetalol; these patients were excluded from any further analyses of changes in arterial pressure and heart rate.

Figure 1 shows the mean systolic, diastolic and mean arterial pressures for the remaining eight patients from the start of the infusion to one hour after discontinuation of the drug. Arterial pressure tended to decrease initially during the first 4 hours of the infusion, reached a trough between hours 4 and 8, and appeared to increase when the infusion was discontinued. Both mean and diastolic arterial pressures showed a significant decrease from baseline values ($p < 0.05$) at 4, 7 and 8 hours. The change in systolic arterial pressure demonstrated a similar trend but there was no significant decrease from the pre-infusion values. Systolic,

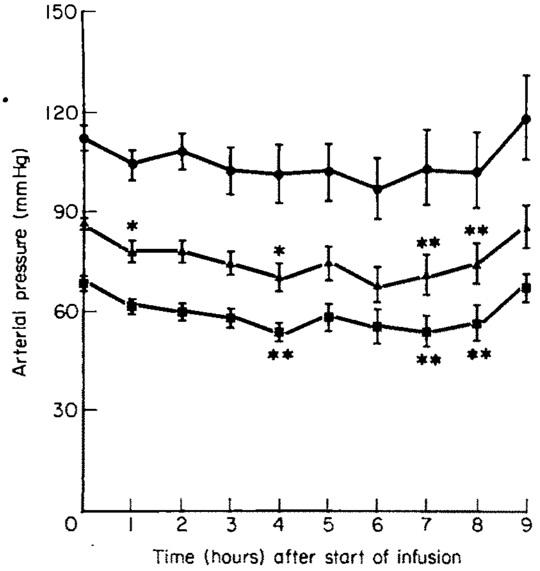


Fig. 1. Mean (SEM) values of systolic (●——●), diastolic (■——■) and mean (▲——▲) arterial pressures during, and after discontinuation of propofol infusion. *, Significant decrease ($p < 0.05$) from baseline value; **, significant decrease ($p < 0.01$) from baseline value.

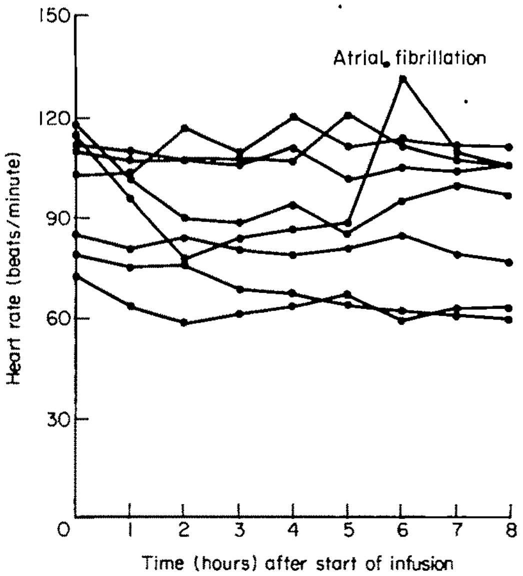


Fig. 2. Heart rate at hourly intervals during propofol infusion.

diastolic and mean arterial pressures one hour after the drug was stopped, all showed a significant increase from the 8-hour values.

A mean arterial pressure of 60 mmHg or less was recorded in six patients at some time during the infusion, although this responded either to intravenous fluid therapy or to a reduction in infusion rate. This hypotension was associated with a recurrence of previously noted atrial fibrillation in patient number 4 and was possibly attributable to the presence of septic shock in patient number 9. In most cases, hypotension was associated with a deep level of sedation.

Changes in infusion rate were generally prompted by alterations in level of sedation but the infusion rate was decreased in three patients because of a continuing downward trend in arterial pressure.

Figure 2 shows the changes in heart rate recorded at hourly intervals during the infusion. Heart rate tended to decrease during the first hour of infusion but this decrease was not maintained.

There were no consistent significant changes in central venous pressure during the period of infusion. However, the rate of intravenous fluid therapy was adjusted to maintain an adequate central venous pressure.

Intravenous fluid requirements varied between 770 and 8150 ml (mean 2604 ml) during the 8-hour period. Patient number 9 (who received 8150 ml) required over 5500 ml within the first 5 hours of infusion. At this stage a pulmonary artery flotation catheter was inserted; the pulmonary capillary wedge pressure was 12 mmHg and a clinical diagnosis of septic shock was made. Cardiac output measurements were not obtained.

In those patients who demonstrated hypotensive episodes there did not appear to be significant impairment of peripheral perfusion, in that core–peripheral temperature gradients and acid–base status remained within normal limits. However, two patients required boluses of frusemide to maintain urine output in the presence of an adequate central venous pressure.

Respiratory variables

There were no marked changes in arterial oxygen tension ($P\mathrm{a}O_2$), arterial carbon dioxide tension ($P\mathrm{a}CO_2$) or (A − a)$D\mathrm{o}_2$ attributable to the effects of the infusion. Airway pressure was not affected and mechanical ventilation was well tolerated in all patients. One patient, number 8, was considered suitable for resumption of spon-

P 24 522

Table 3. Mean (SD) serum cortisol values (nmol/litre) throughout infusion and in response to Synacthen.

	Pre-infusion	4 hours	8 hours	30 minutes after Synacthen	120 minutes after Synacthen
All patients (n = 9)	680 (249)	639 (261)	593 (248)	799* (385)	931* (415)
Patients who received etomidate prior to infusion (n = 4)	597 (102)	618 (221)	577 (212)	655 (238)	759* (212)
Patients who did not receive etomidate (n = 5)	746 (323)	656† (313)	600† (288)	914* (465)	1062* (513)

*Significant increase ($p < 0.05$) from 8-hour (pre-Synacthen) value.
†Significant decrease ($p < 0.05$) from baseline value.

taneous ventilation after the infusion was stopped, and was subsequently extubated.

Adrenocortical function

One patient received hydrocortisone during the study and was excluded from analysis of plasma cortisol values. Results for the remaining nine patients are shown in Table 3. Blood was withdrawn for estimation of plasma cortisol at varying times of the day in different patients but most patients demonstrated increased plasma cortisol values during the infusion (range 249–1198 nmol/litre). When data from all nine patients were analysed collectively, propofol appeared to have no effect on plasma cortisol and the response to Synacthen was normal, with a significant increase in cortisol both 30 and 120 minutes after its administration. However, four patients received etomidate for induction of anaesthesia at times ranging from 3.75 to 7.75 hours before entry to the study. This subgroup entered the study period with cortisol levels lower than in the remaining five patients and, although plasma cortisol remained stable throughout the propofol infusion, the response to the intramuscular Synacthen was obtunded; three patients failed to achieve an absolute increase in cortisol of at least 200 nmol/litre and the mean plasma cortisol values achieved a statistically significant increase from pre-Synacthen levels only at 120 minutes. The five patients who did not receive etomidate had normal Synacthen responses, with significant increases in plasma cortisol at both 30 and 120 minutes after Synacthen, and all five patients achieved increases in plasma cortisol which exceeded 200 nmol/litre. Within this subgroup, however, there was a statistically significant decrease in cortisol levels throughout the period of propofol infusion, although ACTH levels always remained within normal limits.

Two of the four patients who received etomidate had high plasma ACTH levels at the start of the infusion and 4 hours later, while ACTH values in all other patients were normal.

Haematological variables

Only one patient demonstrated lipaemia following propofol infusion for a period of 8 hours; however, this patient received Intralipid 20% simultaneously. There was a significant increase ($p = 0.05$) in prothrombin time from a baseline value of 18 (SEM 1.0) to 19.4 seconds (SEM 1.0) 8 hours following the start of infusion, and a significant increase in urea from 8.7 (SEM 1.3) to 9.6 (SEM 1.4) mmol/litre ($p = 0.02$). There were no significant changes from baseline in any of the other haematological or clinical chemistry variables, and no patient demonstrated a tendency to bleed.

Discussion

Propofol has been investigated extensively both for induction and maintenance of anaesthesia in relatively fit patients (ASA grade 1 or 2) but there has been limited use in patients with significant concurrent disease, with no previous reports of its use in the critically ill. In the present study, propofol proved to be an effective sedative agent when used as a continuous infusion in general intensive care patients who displayed a range of illness severity, as determined by the APACHE II score.

Sedation was readily achieved by an initial bolus dose if required and was maintained in most patients at an acceptable level throughout, with only occasional alterations in infusion rate.

The initial aim of the study was to preserve a comfortable, yet rousable and cooperative state. The use of linear analogue assessment of conscious state and ease of rousability to determine a consciousness score, with the restriction to a single observer for each patient, allowed documentation of smaller differences in level of sedation than previously devised scales.[2] However, there appeared to be considerable individual patient variation in the optimal level of sedation, since some patients became agitated when roused in the intensive care situation while others remained calm and tolerant of the invasive monitoring and therapeutic techniques. Therefore, a subjective assessment of degree of agitation following arousal was also performed and each patient was sedated to that level at which (s)he remained rousable, yet free from agitation when disturbed. On occasions, this required the continual presence of an experienced observer. Once the ideal level of sedation was achieved for each patient, there appeared to be less variability in blood propofol levels for an individual patient during the latter half of the infusion although variations continued to exist between patients.

Propofol infusions have been used for a variety of surgical procedures as part of several different anaesthetic techniques,[9–12] with mean infusion rates in the range 6.2–15.6 mg/kg/hour. The infusion rates used in this study were much lower, with a mean of 1.93 mg/kg/hour. This reflects the aim of the study, which was to maintain patients at a rousable level rather than fully anaesthetised, although the low infusion rates may also be attributable to the fact that all patients in this study were over 55 years of age: older patients appear to require less propofol, both for induction[13] and maintenance of anaesthesia,[11] than younger subjects. Previous work from this centre also suggests that severely ill patients require reduced sedation to produce a given decrease in conscious level[14] and this may have been a contributory factor.

Schüttler *et al.*[15] reported blood propofol levels of 1.64–6.38 μg/ml at induction of sleep and 1.0–2.19 μg/ml on regaining consciousness in healthy volunteers. The range of blood propofol levels during the infusion in the present series (<0.14–1.92 μg/ml) correlates with waking levels in Schüttler's study; this again reflects the intended rousability of patients.

Patients demonstrated a rapid clinical response, as judged by level of sedation, to changes in infusion rate and there was a relatively rapid recovery in most cases after the infusion was stopped. Propofol, with its rapid metabolic clearance and short elimination half-life,[16] appears to be a promising replacement for drugs such as Althesin which provided a controllable level of sedation that could be rapidly and easily varied, with lack of cumulative effects.[2]

Many studies in which propofol has been used for induction and maintenance of anaesthesia, have found respiratory and cardiovascular depression to occur. In the present study, all patients were ventilated mechanically but the lack of requirement for muscle relaxants during the infusion, together with the return of spontaneous ventilation or the need for further sedation to comply with mechanical ventilation after the infusion was stopped, suggest that respiratory depression did occur.

Cardiovascular depression also occurred, with decreases in both systolic and diastolic arterial pressures. Peripheral perfusion appeared to be maintained during hypotension, which suggests that arterial pressure changes were largely attributable to a decrease in peripheral vascular resistance rather than in cardiac output, as shown by a previous study.[17] This would account for the relatively large volumes of fluid required to maintain arterial pressure. Elderly patients are known to be sensitive to the cardiovascular depression induced by propofol[13] but it is possible that severe illness also contributed to the hypotension induced by the drug in our patients.

Propofol, thiopentone and etomidate have all been shown to inhibit cortisol secretion from adrenal cells in a dose-related fashion *in vitro*, although etomidate is 1500 times more potent than thiopentone or propofol.[18] Thiopentone and propofol interfere with the synthesis of cortisol only at very high concentrations which are unlikely to occur in the clinical situation. Etomidate depresses the increase in plasma cortisol but exaggerates the increase in ACTH that occur during the stress response to anaesthesia;[19] cortisol secretion is suppressed well beyond the duration of an etomidate infusion.[20] When given either as a single induction dose or as a short infusion, etomidate decreases the cortisol response to exogenous ACTH administered postoperatively.[21] This finding was confirmed in the present study.

The decrease in plasma cortisol concentration observed during the infusion in those who did not receive etomidate may be attributable to a physiological decrease in the stress response to either severe illness or surgical stimulus which had been initiated several hours before entry to the study; however, the possibility that propofol infusion, or the effect of sedation *per se*, caused this decrease in plasma cortisol cannot be eliminated. Nevertheless, plasma cortisol values remained at relatively high stress levels[22] in most patients and there was a normal response to Synacthen in those who did not receive etomidate. There was, therefore, no evidence of any significant inhibition of adrenal steroidogenesis in association with propofol infusion in the present series.

The fat emulsion Intralipid has previously been demonstrated to alter blood coagulability both *in vitro* and *in vivo*[23,24] by its platelet-like activity and ability to accelerate thrombin generation. Platelet function is also affected[25] and thrombocytopenia in association with the use of Intralipid has been described.[26] Sear[27] reported no alterations in coagulation during maintenance of anaesthesia with propofol for a duration of 45 minutes. In this series, the only change was a minor increase in prothrombin time which may, in any case, be attributable to a variety of causes in critically ill or post-operative patients.

In conclusion, propofol appeared to be a useful sedative agent by infusion in 10 critically ill patients with a variety of severity of illness. The desired level of sedation for individual subjects was achieved readily by adjustment of the infusion rate, and discontinuation of the drug was followed by a relatively rapid recovery. Critically ill patients, however, may be particularly sensitive to the cardiovascular depressant effects of the drug, even at low doses, and this, together with possible respiratory depression, warrants further investigation in similar patients. It is conceivable that greater difficulties might arise in the absence of continuous supervision of both level of sedation and infusion rate.

Acknowledgments

The authors thank ICI for supplies of propofol and for their help in this project, all staff in the Intensive Care Unit for their patience and assistance and Mrs I. Fergusson and Mrs M. Groves for typing the manuscript.

References

1. Bion JF, Ledingham IMcA. Sedation in intensive care—a postal survey. *Intensive Care Medicine* 1987 (in press).
2. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphaxolone–alphadolone. *British Medical Journal* 1974; **2:** 656–9.
3. Edbrooke DL, Newby DM, Mather SJ, Dixon AM, Hebron BS. Safer sedation for ventilated patients. A new application for etomidate. *Anaesthesia* 1982; **37:** 765–71.
4. Watt I, Ledingham IMcA. Mortality amongst multiple trauma patients admitted to an intensive therapy unit. *Anaesthesia* 1984; **39:** 973–81.
5. Lambert A, Mitchell R, Frost J, Ratcliffe JG, Robertson WR. Direct in vitro inhibition of adrenal steroidogenesis by etomidate. *Lancet* 1983; **2:** 1085–6.
6. Fraser R, Watt I, Gray CE, Ledingham IMcA, Lever AF. The effect of etomidate on adrenocortical function in dogs before and during hemorrhagic shock. *Endocrinology* 1984; **115:** 2266–70.
7. Glen JB, Hunter SC. Pharmacology of an emulsion formulation of ICI 35868. *British Journal of Anaesthesia* 1984; **56:** 617–25.
8. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Critical Care Medicine* 1985; **13:** 818–29.
9. Grounds RM, Morgan M, Lumley J. Some studies on the properties of the intravenous anaesthetic, propofol ('Diprivan')—a review. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 90–5.
10. MacKenzie N, Grant IS. Propofol ('Diprivan') for continuous intravenous anaesthesia. A comparison with methohexitone. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 70–5.
11. Hilton P, Dev VJ, Major E. Intravenous anaesthesia with propofol and alfentanil. The influence of age and weight. *Anaesthesia* 1986; **41:** 640–3.
12. Kay B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41:** 589–95.
13. Dundee JW, Robinson FP, McCollum JSC, Patterson CC. Sensitivity to propofol in the elderly. *Anaesthesia* 1986; **41:** 482–5.
14. Bion JF, Logan BK, Newman PM, Brodie MJ, Oliver JS, Aitchison TC, Ledingham IMcA. Sedation in intensive care; morphine and renal function. *Intensive Care Medicine* 1986; **12:** 359–65.
15. Schüttler J, Stoeckel H, Schwilden H. Pharmacokinetic and pharmacodynamic modelling of propofol ('Diprivan') in volunteers and surgical patients. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 53–4.

16. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 45–50.
17. Grounds RM, Twigley AJ, Carli F, Whitwam JG, Morgan M. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia* 1985; **40:** 735–40.
18. Robertson WR, Reader SCJ, Davison B, Frost J, Mitchell R, Kayte R, Lambert A. On the biopotency and site of action of drugs affecting endocrine tissues with special reference to the antisteroidogenic effect of anaesthetic agents. *Postgraduate Medical Journal* 1985; **61**(Suppl. 3): 145–51.
19. Fragen RJ, Shanks CA, Molteni A, Avram MJ. Effects of etomidate on hormonal responses to surgical stress. *Anesthesiology* 1984; **61:** 652–6.
20. Moore RA, Allen MC, Wood PJ, Rees LH, Sear JW. Peri-operative endocrine effects of etomidate. *Anaesthesia* 1985; **40:** 124–30.
21. Wagner RL, White PF. Etomidate inhibits adrenocortical function in surgical patients. *Anesthesiology* 1984; **61:** 647–51.
22. Finlay WEI, McKee JI. Serum cortisol levels in severely stressed patients. *Lancet* 1982; **1:** 1414–5.
23. Reid DJ, Ingram GIC. Changes in blood coagulation during infusion of Intralipid. *Clinical Science* 1967; **33:** 399–407.
24. Amris CJ, Brockner J, Larsen V. Changes in the coagulability of blood during the infusion of Intralipid. *Acta Chirurgia Scandinavica* 1964; **325** (Suppl.): 70–4.
25. Burnham WR, Heptinstall S, Cockbill SR, Harrison S. Blood platelet behaviour during infusion of an Intralipid-based intravenous feeding mixture. *Postgraduate Medical Journal* 1982; **58:** 152–5.
26. Lipson AH, Pritchard J, Thomas G. Thrombocytopenia after Intralipid infusion in a neonate. *Lancet* 1974; **2:** 1462–3.
27. Sear JW, Uppington J, Kay NH. Haematological and biochemical changes during anaesthesia with propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 165–8.

Anaesthesia, 1987, Volume 42, pages 938–943

One lung anaesthesia

Cardiovascular and respiratory function compared during conventional ventilation and high frequency jet ventilation

J. JENKINS, E. W. J. CAMERON, A. C. MILNE AND R. M. HUNTER

Summary

Ten patients about to undergo left-sided thoracotomy for carcinoma of the lung were entered into a crossover trial to compare cardiovascular and respiratory function during high frequency jet ventilation and conventional mechanical ventilation for one lung anaesthesia. All patients were anaesthetised with a standard technique using double lumen tubes and placed in the lateral position with the left chest open.

The results showed no significant differences with regard to ventilation sequence but one lung high frequency jet ventilation gave higher values than one lung conventional ventilation for shunt ($p < 0.01$) *and positive end expiratory pressure* ($p < 0.05$) *and lower peak inflation pressure values* ($p < 0.01$). *There were no significant differences in cardiac output, pulmonary capillary wedge pressure, arterial carbon dioxide or available oxygen.*

Surgical conditions were satisfactory during both methods of ventilation and satisfactory gas exchange occurred. It was, however, more difficult to assess adequacy of ventilation during high frequency jet ventilation and the routine use of this method of ventilation is not recommended during one lung anaesthesia.

Key words

Anaesthesia; thoracic.
Ventilation; high frequency jet, intermittent positive pressure.

One lung anaesthesia (OLA) with double lumen tubes is the usual anaesthetic technique used in British thoracic surgical units[1] to protect the dependent lung and improve surgical access. However, during OLA the shunt through the collapsed lung may be greater than 50% of cardiac output[2,3] and the shunt increases further when high inflation pressures are employed.[4] It has also been shown that, although arterial oxygen tension ($Pa\text{o}_2$) is substantially lowered during OLA, oxygen saturation ($Sa\text{o}_2$) and content are but slightly changed[5] and, therefore, cardiac output (Q_t) is the crucial element in the maintenance of oxygen delivery during OLA (available oxygen = haemoglobin (g/dlitre) × 1.34 × cardiac output × oxygen saturation). Oxygen delivery is not improved by the use of positive end expiratory pressure (PEEP).[6]

An anaesthetic technique which disturbs cardiac output minimally during OLA should

---

J. Jenkins,* MB, ChB, BSc, FFARCS, Senior Registrar, E.W.J. Cameron, BSc, MB, ChB, FRCSE, A.C. Milne, MB, ChB, FFARCS, Consultants, City Hospital, Greenbank Drive, Edinburgh EH10 5SB, R.M. Hunter, BSc, MSc, Research Associate, Medical Statistics Unit, Medical School, Teviot Place, Edinburgh EH8 9AG.
* Present address: Consultant, Eastern General Hospital, Seafield Street, Edinburgh EH6 7LN.

0003–2409/87/090938 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

therefore maximise oxygen delivery. Since airway pressures are low during high frequency jet ventilation (HFJV) and phases of high inflation pressure do not occur, HFJV should offer advantages over intermittent positive pressure ventilation during OLA. The dangers of barotrauma[7,8] and depression of cardiac output[9] are thus avoided.

Air entrainment techniques have been used for bronchoscopy,[10] laryngeal and tracheal surgery[11-16] and, more recently, for thoracic surgery.[17] The effects on oxygen delivery of HFJV during OLA using anaesthetic gases have not been reported previously. Anaesthetic agents are known to affect ventilation–perfusion ratios but the advantages of an inhalational technique allow smaller doses of intravenous agents to be used and thereby facilitate a more rapid recovery.

Methods

Ethical approval was obtained for the study. Ten patients scheduled for left thoracotomy for bronchogenic carcinoma were studied. They were all ASA grade 1 or 2 and gave informed consent. They were divided randomly into two groups of five. The lungs of each group were to be ventilated in a different sequence in an attempt to allow for changes which may occur in the lung with time[18] and during different types of ventilation.

All patients were premedicated with papaveretum 15–20 mg intramuscularly one hour preoperatively. Anaesthesia was induced using a sleep dose of thiopentone, phenoperidine 2 mg and alcuronium 20 mg. A right-sided double lumen bronchial tube (Mallinckrodt Bronchocath) was passed and its position checked with a fibreoptic bronchoscope. Maintenance of anaesthesia was with 50% nitrous oxide in oxygen throughout the entire study. Only one patient required a second dose of phenoperidine 2 mg. Monitoring consisted of electrocardiogram, direct right radial artery pressure and a balloon tipped flow-directed pulmonary artery catheter passed via the right internal jugular vein. An intravenous infusion of Ringer's lactate was started at 250 ml/hour. The position of the pulmonary artery catheter was checked by chest X ray and in all cases the tip wedged and lay in a branch of the right pulmonary artery. Throughout the study patients were placed in the lateral position on a heated water blanket with the left chest open. The sequence of ventilation for group A was two lung (TL) IPPV, one lung (OL) IPPV and then OL HFJV. For group B it was TL IPPV, OL HFJV and then OL IPPV.

Intermittent positive pressure ventilation was from a Penlon Nuffield 400 ventilator set to deliver an expired tidal volume of 650 ml at a rate of 14 breaths/minute and an inspiratory: expiratory ratio of 1:2. High frequency jet ventilation was from an Acutronic MK800 ventilator set at a rate of 150–200 breaths/minute, minute volume 10–15 litres via a 16-G Angiocath. A blender (Bird 3M) delivered 50% nitrous oxide in oxygen to the jet ventilator and this mixture was also delivered at 8 litres/minute for entrainment (Fig. 1).

The following measurements were made after 15 minutes in each mode of ventilation: respiratory rate, minute ventilation, positive end expiratory pressure, peak inflation pressure,

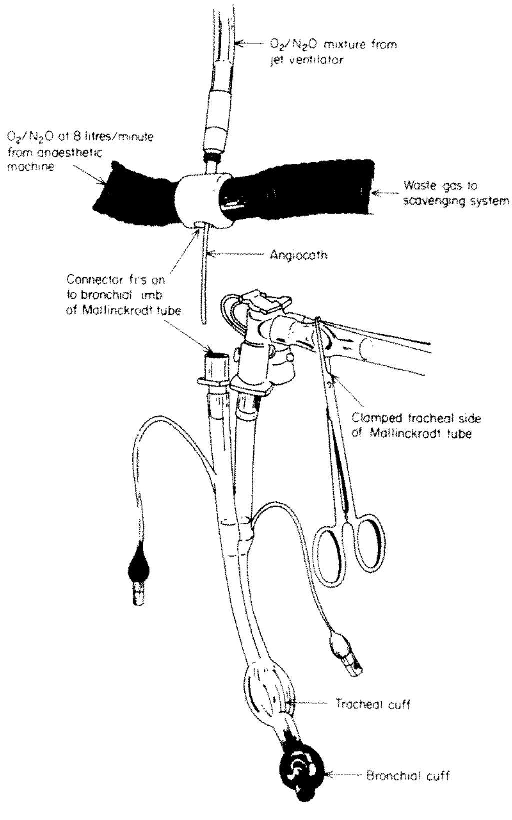

O_2/N_2O mixture from jet ventilator
O_2/N_2O at 8 litres/minute from anaesthetic machine
Waste gas to scavenging system
Angiocath
Connector fits on to bronchial limb of Mallinckrodt tube
Clamped tracheal side of Mallinckrodt tube
Tracheal cuff
Bronchial cuff

Fig. 1. Drawing to show attachments of bronchial tube to Acutronic HFJV and to conventional lung ventilator.

radial and pulmonary arterial gases, cardiac output (twice), heart rate, radial artery pressure, pulmonary artery capillary wedge pressure and core temperature. During IPPV, airway pressures were recorded from a calibrated manometer (MIE) mounted on the inspiratory limb, and expired minute volume with a calibrated respirometer (Medishield, Wright) on the expiratory limb of the patient circuit. Airway pressure during HFJV was measured using a 12-G saline-filled catheter advanced to the tip of the right side of the bronchial tube. All blood gas samples were kept on ice until analysed (Radiometer Copenhagen ABL2). Cardiac output was measured by the thermodilution technique using ice cold saline and the results analysed with an Edwards Cardiac Output Computer. During IPPV the iced saline was injected at the end of expiration. Two measurements of cardiac output were made during stable conditions for each mode of ventilation and single measurements were made of all other variables. Radial and pulmonary artery pressures were measured with a transducer (Gould P50) and displayed on a monitor (Simonsen and Weel). No surgery was undertaken whilst the study was in progress.

Statistical method

Standard statistical methods for the analysis of crossover trials were employed.[19] The presence of a period effect was investigated by comparing the difference between changes from baseline for one treatment and changes from baseline for the other treatment for the two treatment order groups, i.e. (OL HFJV–TL IPPV) – (OL IPPV–TL IPPV) was calculated for sequence A patients and also for sequence B patients. A two-sample test for a difference between sequence A patients and sequence B patients, tests for a period effect while allowing for a treatment difference. Similarly, tests for a treatment effect were performed by considering changes from baseline to period 1 and period 2 measurements, i.e. (period 2–TL IPPV) – (period 1–TL IPPV) was calculated for both treatment order groups. A two-sample test between the two treatment order groups tests for a difference in treatments while allowing for a period effect. As the sample size is very small, an assumption of no treatment–period interaction has had to be made.

For all variables except mean arterial pressure (MAP), cardiac index (CI) and shunt ($\dot{Q}_s/\dot{Q}_t$), differences were normally distributed and the two results were analysed using two-sample *t*-tests.[20] The Wilcoxon rank-sum test was used for MAP, CI and $\dot{Q}_s/\dot{Q}_t$.

Results

No significant period effects were found: there was no significant difference between group A and group B patients as a result of the sequence of ventilation. The results from the two groups were therefore combined (Table 1) to show all the variables for TL IPPV, OL IPPV and OL HFJV.

The results of the two-sample *t*-test and Wilcoxon rank-sum tests for treatment effects are given in Tables 2 and 3. Significant differences at the 1% level were found for PIP (OL HFJV had lower values than OL IPPV) and for

Table 1. Means and standard deviations for cardiovascular and respiratory variables.

	Two lung ventilation		One lung ventilation			
	IPPV		IPPV		HFJV	
Variable	Mean	(SD)	Mean	(SD)	Mean	(SD)
HR, beats/minute	83.3	13.3	79.5	12.0	78.5	10.6
MAP, mmHg	81.2	15.9	78.1	16.7	80.6	15.8
PCWP, mmHg	20.5	6.5	22.0	8.6	24.6	8.8
LVSWI, g m/sq. m	36.5	17.8	38.6	20.7	38.3	23.5
CI, litres/minute/sq. m	3.8	2.2	3.5	1.9	3.9	1.9
$Pa\text{O}_2$, kPa	21.5	5.1	11.6	6.6	9.8	3.6
$Pa\text{CO}_2$, kPa	5.5	0.7	5.6	0.9	6.5	1.5
$Sa\text{O}_2$, %	98.5	0.9	91.6	5.2	88.3	7.9
$\dot{Q}_s/\dot{Q}_t$, %	15.4	5.6	32.9	13.4	42.4	16.8
Av O_2, ml/minute × 10^{-1}	114.2	71.0	98.8	60.8	106.7	60.1
PEEP, kPa	0.01	0.03	0.0	0.0	0.78	0.66
PIP, kPa	1.56	0.52	2.56	0.49	0.89	0.64
$P\bar{v}\text{O}_2$, kPa	6.4	0.7	5.2	0.7	5.4	0.4

Table 2. Two-sample *t*-tests for treatment effects.

Variable	Mean treatment difference*	95% confidence interval	Significance
HR	−1.0	(−6.6, 7.6)	0.88
PCWP	2.6	(−0.3, 5.5)	0.06
LVSWI	4.7	(−3.3, 12.8)	0.18
$P\text{ao}_2$	−1.8	(−4.8, 1.4)	0.20
$P\text{aco}_2$	0.9	(−0.2, 2.0)	0.11
$S\text{ao}_2$	−3.3	(−7.9, 1.3)	0.12
Av O_2	7.9	(−2.4, 18.2)	0.11
PEEP	0.78	(0.17, 1.40)	0.02
PIP	−1.67	(2.48, 0.85)	$p < 0.01$

* Positive difference indicates HFJV higher in value than IPPV; negative difference, *vice versa*. (Units, see Table 1.)

Table 3. Wilcoxon rank-sum tests for treatment effects.

Variable	Median treatment difference*	Significance
MAP	0.5	0.5
CI	0.7	0.22
$\dot{Q}_s/\dot{Q}_t$	7.7	0.008

* Positive difference indicates HFJV higher in value than IPPV; negative difference, *vice versa*.

shunt (OL HFJV had higher values than OL IPPV). Differences in PEEP were significant at the 5% level (OL HFJV had higher values than OL IPPV). There was no significant difference between values for $\dot{Q}_t$, PCWP, $P\text{aco}_2$, $S\text{ao}_2$ and Av O_2 during OL IPPV and OL HFJV.

Discussion

The crossover design of this trial was intended to allow for changes which are known to occur in the lungs and blood gases over a period of time after the start of OLA.[18] Analysis showed that ventilation sequence and time from the start of one lung anaesthesia did not have a significant effect on our results which, therefore, relate directly to the method of ventilation.

We consider that the most important function of double lumen tubes during thoracic surgery is the protection of the dependent lung from contamination and, for this reason, we kept the cuffs on the bronchial tubes inflated at all times. We do not consider that the pressure and gas flow generated during OL HFJV are adequate to protect the dependent lung if the bronchial cuff is deflated, as has been suggested for the prevention of aspiration.[21] For this reason our study involved either TL IPPV or OLA without any insufflation of the superior lung, in contrast to that advocated by El-Baz *et al.*[22] in their technique of modified OLA.

The use of a nitrous oxide–oxygen mixture delivered both for entrainment and to the jet has not been described previously. It avoids the routine use of 100% oxygen which may produce hyperoxygenation and it reduces the requirement for an intravenous anaesthetic technique and thereby facilitates rapid recovery at the end of the operation. There were no significant changes in heart rate or mean arterial pressure during the study and no problems with awareness.

No PEEP was generated during IPPV but a significant level was measured during HFJV. Our results confirm the findings of others[6] that PEEP in the ventilated dependent lung diverts blood flow to the non-ventilated lung. This diversion of blood flow was seen during both OL IPPV and OL HFJV. The unintentional generation of PEEP during HFJV has been noted by others[23–26] and attributed to expiratory flow limitation. Glenski[27] used a bias tube of variable diameter to alter expiratory flow resistance during high frequency ventilation. Our expiratory limb was large in comparison to that used by Glenski and we would not have expected this to cause expiratory flow resistance. The fact that the inspiratory:expiratory ratio was set at 0.3 on the HFJ ventilator parallels more closely the conditions described by Rouby.[23] He showed that expiratory flow decays exponentially with a time constant longer than the duration of expiration. Gas trapping therefore occurs and PEEP is generated. The degree of PEEP depends more on the inspiratory:expiratory ratio and driving pressure than on frequency. Sladen *et al.*[28] found that PEEP was necessary during HFJV to prevent atelectasis. However, this expansion of lung volume may not occur with an open thorax and when only one dependent lung is ventilated. In these circumstances OL HFJV would appear to have the same effect as OL IPPV with PEEP in the diversion of blood flow to the superior non-ventilated lung with resultant increased shunt. This hypothesis is given support by estimated mean airway pressures of 0.85 kPa during OL IPPV, 0.86 kPa during OL HFJV and 0.53 kPa during TL IPPV. Thus, despite higher peak pressures during OL IPPV, the mean airway pressure is the same as during OL HFJV. Mean pulmonary capillary wedge pressure increased from 20.5 mmHg during TL IPPV to 22 mmHg during OL IPPV and 24.6 mmHg during OL HFJV. These figures are not significantly different ($p = 0.06$) but they are in keeping with the increase in mean airway pressure during both methods of one lung ventilation.

The relatively small deterioration in Pa_{O_2} during OL HFJV in comparison with the significant increase in the shunt fraction, suggests that the mixed venous P_{O_2} ($P\bar{v}_{O_2}$) increased. The difference between the $P\bar{v}_{O_2}$ during TL IPPV and both methods of one lung ventilation was highly significant but there was no significant difference between $P\bar{v}_{O_2}$ during OL HFJV and OL IPPV. It cannot, therefore, be postulated that hypoxic vasoconstriction in the unventilated lung was reduced to account for the increase in shunt.

Thus the theoretical benefits of HFJV on the cardiovascular system are outweighed by the effects of mean airway pressure increasing shunt to the unventilated lung during one lung anaesthesia. Adequate gas exchange can be maintained during OL HFJV but the difficulties in this assessment contraindicate the routine use of this method of ventilation.

Acknowledgments

The authors thank Dr P. Tweeddale and her staff for performing blood gas analyses, Miss J. Holywell and Mrs G. Lawrence for typing the manuscript and the staff of the thoracic theatre, City Hospital for their assistance in the execution of the study.

References

1. Pappin JC. The current practice of endobronchial intubation. *Anaesthesia* 1979; **34:** 57–64.
2. Torda TA, McCulloch CH, O'Brien HD, Wright JS, Horton DA. Pulmonary venous admixture during one-lung anaesthesia. The effect of inhaled oxygen tension and respiration rate. *Anaesthesia* 1974; **29:** 272–9.
3. Kerr JH, Crampton Smith A, Prys-Roberts C, Meloche R, Foëx P. Observations during endobronchial anaesthesia. II. Oxygenation. *British Journal of Anaesthesia* 1974; **46:** 84–92.
4. Khanam T, Branthwaite MA. Arterial oxygenation during one-lung anaesthesia. 1. A study in man. *Anaesthesia* 1973; **28:** 132–8.
5. Aalto-Setälä M, Heinonen J. One lumen versus double lumen endobronchial tubes in thoracic anaesthesia: a comparison of blood gas tensions. *Annales Chirurgiae et Gynaecologiae Fenniae* 1974; **63:** 276–83.
6. Aalto-Setälä M, Heinonen J, Salorinne Y. Cardiorespiratory function during thoracic anaesthesia: a comparison of two-lung ventilation and one-lung ventilation with and without PEEP. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 287–95.
7. Kirkby RR. Ventilatory support and pulmonary barotrauma. *Anesthesiology* 1979; **50:** 181–2.
8. De Latoere FJ, Tomasa A, Klamburg J, Leon C, Soler M, Ruis J. Incidence of pneumothorax and pneumomediastinum in patients with aspiration pneumonia requiring ventilatory support. *Chest* 1977; **72:** 141–4.
9. Abu Dbai J, Flatau E, Lev A, Kohn D, Mouris-Hass I, Barzilay E. The use of conventional ventilators for high frequency positive pressure ventilation. *Critical Care Medicine* 1983; **11:** 356–8.
10. Sanders RD. Two ventilating attachments for bronchoscopes. *Delaware Medical Journal* 1967; **39:** 170–5.
11. Lee P, English ICW. Management of anaesthesia during tracheal resection. *Anaesthesia* 1974; **29:** 305–6.
12. Eriksson I, Sjöstrand U. Effects of high-frequency positive-pressure ventilation (HFPPV) and general anesthesia on intrapulmonary gas distribution in patients undergoing diagnostic bronchoscopy. *Anesthesia and Analgesia* 1980; **59:** 585–93.
13. Albert SN, Shibuya J, Albert CA. Ventilation with an oxygen injector for suspension laryngoscopy under general anaesthesia. *Anaesthesia and Analgesia* 1972; **51:** 866–70.
14. Eriksson I, Nilsson LG, Nordstrom S, Sjöstrand U. High-frequency positive-pressure ventilation (HFPPV) during transthoracic resection of tracheal stenosis and during peroperative bronchoscopic examination. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 113–9.
15. Babinsky M, Smith RB, Klain M. High-frequency jet ventilation for laryngoscopy. *Anesthesiology* 1980; **52:** 178–80.
16. Borg U, Eriksson I, Sjöstrand U. High-frequency positive-pressure ventilation (HFPPV): a review based upon its use during bronchoscopy and for laryngoscopy and microlaryngeal surgery under general anesthesia. *Anesthesia and Analgesia* 1980; **59:** 594–603.

17. Hildebrand PJ, Prakash D, Cosgrove J, Wilson JJ, Coppel DL. High frequency jet ventilation. A method for thoracic surgery. *Anaesthesia* 1984; **39:** 1091–5.
18. Fisher WP, Friday CD, Read RC. Changes in arterial oxygenation and pulmonary shunt during thoracotomy with endobronchial anesthesia. *Journal of Thoracic and Cardiovascular Surgery* 1982; **83:** 523–31.
19. Hills M, Armitage P. The two period cross over trial. *Statistician* 1982; **31:** 119–30.
20. Documenta Geigy. *Scientific tables, statistical methods*. Manchester: Geigy Pharmaceutical Co., 1962: 112.
21. Klain M, Keszler H, Stool S. Transtracheal high frequency jet ventilation prevents aspiration. *Critical Care Medicine* 1983; **11:** 170–2.
22. El-Baz NM, Kittle CF, Faber LP, Welsher W. High-frequency ventilation with an uncuffed endobronchial tube. A new technique for one-lung anesthesia. *Journal of Thoracic and Cardiovascular Surgery* 1982; **84:** 823–8.
23. Rouby JJ. Jet ventilation à haute frequences: aspects, techniques et mechanisme des éxchanges gazeux dans les insuffisances respiratoires aigues. In: Bourgain JL, Lienhart A, Viars P, eds. *Ventilation à haute frequence*. Paris: Librairc Arnette, 1983.
24. Rehder K, Didier EP. Gas transport and pulmonary perfusion during high-frequency ventilation in humans. *Journal of Applied Physiology* 1984; **57:** 1231–7.
25. Crawford M, Rehder K. High-frequency small-volume ventilation in anesthetized humans. *Anesthesiology* 1985; **62:** 298–304.
26. Goldstein D, Slutsky AS, Ingram RH, Westerman P, Venegas J, Drazen J. CO_2 elimination by high frequency ventilation (4 to 10 Hz) in normal subjects. *American Review of Respiratory Diseases* 1981; **123:** 251–5.
27. Glenski JA, Crawford M. High frequency, small volume ventilation during thoracic surgery. *Anesthesiology* 1986; **64:** 211–4.
28. Sladen A, Guntupalli K, Klain M, Romano R. High frequency jet ventilation and conventional ventilation: a comparison of cardiorespiratory parameters. In: Scheck PA, ed. *Perspectives in high frequency ventilation. International Symposium Proceedings* (Developments in Critical Care Medicine and Anaesthesiology). Boston, MA: Kluwer/Nijhoff, 1983: 305–8.

Anaesthesia, 1987, Volume 42, pages 944–949

The effects of vecuronium on intra-ocular pressure

R. K. MIRAKHUR, W. F. I. SHEPHERD, G. G. LAVERY AND P. ELLIOTT

Summary

The effects of vecuronium on intra-ocular pressure were investigated in doses of 0.1 mg/kg during steady state anaesthesia (n = 5), 0.1 mg/kg as part of a normal sequence induction preceded by thiopentone (n = 10), and 0.15 mg/kg as part of a rapid sequence induction with vecuronium administered prior to thiopentone (n = 10). Administration of vecuronium during steady state anaesthesia was associated with a significant decrease. Vecuronium produced a small reduction in pressure during a normal sequence induction, following a significant reduction after thiopentone. Tracheal intubation during normal sequence and rapid sequence inductions produced increases in pressure above the pre-intubation value (significantly so in the case of normal sequence induction); however, the intra-ocular pressure always remained below the pre-induction value, which suggests that vecuronium 0.15 mg/kg is a suitable relaxant as part of a rapid sequence induction technique where the use of suxamethonium is contraindicated.

Key words

Anaesthetic techniques; rapid sequence induction.
Neuromuscular relaxants; vecuronium.

The success of ophthalmic surgery, particularly where the globe is opened, depends to a large extent on good control of intra-ocular pressure (IOP) not only during maintenance but also at induction of anaesthesia. This is usually achieved with controlled ventilation of the lungs, facilitated by the use of non-depolarising muscle relaxants. Non-depolarising muscle relaxants are also advocated as part of a modified rapid sequence induction in patients with a full stomach, where the use of suxamethonium is contraindicated, as in patients with perforated eye injuries.[1] Non-depolarising relaxants such as pancuronium have to be administered in relatively large doses to hasten their onset of action in these situations. This may be associated not only with the occurrence of undesirable side effects but also with a prolonged block.[2]

Vecuronium is a non-depolarising agent which is comparatively short-acting and free of any cardiovascular or other side effects, even when used in relatively large doses,[3–5] and it would appear to be suitable for use in ophthalmic surgery. There are some reports of effects of vecuronium on IOP during a routine induction[6,7] and a recent report[8] about its effects on IOP during steady state anaesthesia, but there is no information about its effects on IOP when used as part of a rapid sequence induction. In the present study the effects of vecuronium on IOP were studied during steady state anaesthesia, during a normal induction

---

R.K. Mirakhur, MD, PhD, FFARCS, Consultant, W.F.I. Shepherd, FRCS, Consultant Ophthalmologist and Senior Lecturer, G.G. Lavery, FFARCS, Senior Registrar, P. Elliott, MD, FFARCS, Consultant, Departments of Anaesthetics and Ophthalmology, Royal Victoria Hospital and the Queen's University of Belfast.

0003–2409/87/090944 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

sequence and during a rapid sequence induction.

Patients and methods

Adult patients scheduled to undergo elective ophthalmic surgery were included in the study after their informed consent and approval from the regional ethical committee had been obtained. Patients who suffered from pre-existing elevated intra-ocular pressure or systemic hypertension were excluded from the study. All received diazepam 10–15 mg orally as premedication. Intra-ocular pressure was measured using a Perkins' hand-held applanation tonometer in the eye not to be operated upon. Heart rate and blood pressure were monitored using an ECG and an oscillotonometer (Dinamap).

Steady state anaesthesia. Anaesthesia was induced in five patients with thiopentone 4–5 mg/kg and fentanyl 4–5 μg/kg following measurement of IOP while awake (under local anaesthesia). The larynx was sprayed with 4% lignocaine and tracheal intubation carried out without the use of a muscle relaxant. Anaesthesia was maintained with 66% nitrous oxide in oxygen and ventilation adjusted to maintain the end tidal carbon dioxide concentration at 4.5–5.0%. Patients were given vecuronium in a dose of 0.1 mg/kg when all parameters had been stable for at least 10 minutes. The IOP, heart rate and systolic blood pressure were measured immediately prior to and at 1, 2, 3, 4, 5 and 10 minutes after administration of the relaxant.

Normal sequence induction. Anaesthesia was induced with fentanyl 2 μg/kg and thiopentone 4–5 mg/kg followed one minute later by vecuronium 0.1 mg/kg. Tracheal intubation was performed 3 minutes after vecuronium administration. IOP, heart rate and systolic blood pressure were measured prior to induction of anaesthesia (under local anaesthesia), after thiopentone, before intubation, immediately after intubation and one and 2 minutes later. Anaesthesia was maintained thereafter with nitrous oxide, oxygen and halothane. Ten patients were studied in this manner.

Rapid sequence induction. Patients were preoxygenated for 5 minutes, during which time they received fentanyl 2 μg/kg, following measurement of baseline IOP (under local anaesthesia). Vecuronium was then administered in a dose of 0.15 mg/kg followed by thiopentone 5 mg/kg as soon as signs of muscle weakness, such as inability to keep the eyes open, appeared. Cricoid pressure was applied at the loss of eyelash reflex and tracheal intubation and cuff inflation were performed 30 seconds after thiopentone administration. Ventilation was not assisted until the airway had been secured. The IOP, heart rate and systolic blood pressure were measured after thiopentone administration, immediately after intubation and one and 2 minutes later when the study was terminated. Anaesthesia was maintained thereafter as in the normal sequence induction group. Ten patients were studied using this induction sequence.

The IOP, heart rate and blood pressure changes in each group were subjected to a paired *t*-test to determine the statistical significance of the results

Results

The physical characteristics of the patients in the three groups are shown in Table 1. Patients in the steady state group were generally younger, and those in the normal sequence induction group older, than patients in the rapid sequence induction group. The baseline IOP was, however, comparable in all the groups.

IOP during steady state anaesthesia. The IOP during steady state anaesthesia was significantly lower ($p < 0.01$) at an average of 5.4 mmHg, in comparison to the awake value of 13.4 mmHg. Administration of vecuronium 0.1 mg/kg produced a further reduction in IOP throughout the 10-minute period of study (Fig. 1). The decrease was significant ($p < 0.01$) over the first 3 minutes and the lowest average value of 3.4 mmHg was reached at this time. There were no significant changes in heart rate and systolic blood pressure during the study period, as can be seen from Fig. 1.

The IOPs during normal sequence and rapid sequence induction techniques are given in Table 2.

IOP during normal sequence induction. Administration of thiopentone produced a highly significant ($p < 0.001$) decrease in IOP from 13.4 to 6.6 mmHg, a decrease of over 50%. Administration of vecuronium produced a further small decrease. Tracheal intubation was associated with an increase in IOP which was significant ($p < 0.01$) in comparison to the

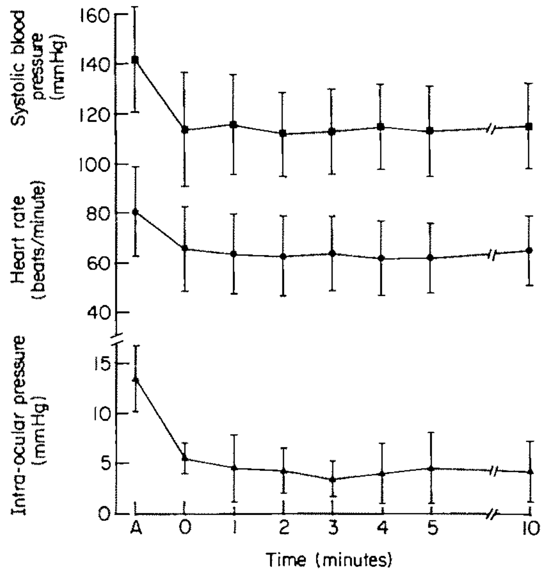


Fig. 1. Mean (SD) intra-ocular pressure, heart rate and systolic blood pressure with vecuronium administration during steady state anaesthesia. A, Awake; 0, prior to vecuronium; 1–10, time (minutes) after vecuronium administration; ▲, intra-ocular pressure; ●, heart rate; ■, systolic blood pressure.

Table 1. Physical characteristics of patients.

Characteristic	Patient group Steady state anaesthesia ($n = 5$)	 Normal sequence induction ($n = 10$)	 Rapid sequence induction ($n = 10$)
Mean (SD) age, years	35 (17.9)	64 (13.0)	44 (18.7)
Mean (SD) weight, kg	65 (16.7)	64 (8.4)	71 (9.6)
Mean (SD) baseline IOP, mmHg	13.4 (5.3)	13.4 (2.1)	13.7 (3.1)

Table 2. Mean (SD) IOPs during induction.

Time	IOP, mmHg Normal sequence	 Rapid sequence
Control (awake)	13.4 (2.11)	13.7 (3.05)
After induction	6.6 (2.95)*	
Before intubation	5.2 (1.87)*	9.7 (2.58)*
Following intubation	11.3 (5.03)†	12.9 (4.35)
After 1 minute	9.1 (3.51)*	11.9 (3.31)
After 2 minutes	8.7 (3.02)*	10.2 (3.32)*

* Significantly different from control.
† Significantly different from value before intubation.

value immediately before it. However, the IOP was not significantly different from the awake state and was in fact still lower than it. The IOP decreased over the next 2 minutes and was significantly lower ($p < 0.001$) than the awake value at these times.

IOP during rapid sequence induction. Thiopentone administration was again associated with a significant ($p < 0.01$) decrease in IOP from 13.7 to 9.7 mmHg. Tracheal intubation was associated with an increase in IOP but this was not significant in comparison to either the control IOP or the pressure immediately prior to intubation. In fact, the IOP never exceeded the control value. IOP decreased subsequently over the next 2 minutes and was significantly below ($p < 0.02$) the control IOP 2 minutes after intubation.

Heart rates and systolic blood pressures during the two induction techniques, are given in

Table 3. Mean (SD) heart rate and systolic blood pressure during normal sequence and rapid sequence induction employing vecuronium.

Time	Heart rate, beats/minute		Systolic blood pressure, mmHg	
	Normal sequence	Rapid sequence	Normal sequence	Rapid sequence
Control (awake)	81 (14.7)	85 (17.9)	160 (21.2)	150 (22.2)
After induction	88 (23.0)		144 (15.1)*	
Before intubation	81 (14.2)	96 (20.1)	142 (26.4)	152 (24.4)
Following intubation	100 (21.3)*†	107 (21.5)*	171 (34.8)†	165 (24.3)*†
After 1 minute	91 (18.3)*	102 (18.4)*	173 (26.7)	165 (30.7)*†
After 2 minutes	87 (20.9)	97 (18.3)	163 (28.2)	153 (26.8)

* Significantly different from control.
† Significantly different from value before intubation.

Table 4. Mean (SD) onset and duration of clinical relaxation (see text for details).

Group	Onset, seconds	Duration, minutes
Normal sequence group (vecuronium 0.1 mg/kg)	278 (74)	29 (7.2)
Rapid sequence group (vecuronium 0.15 mg/kg)	166 (29.7)	47 (5.7)

Table 3. Administration of thiopentone produced increases in heart rate and decreases in blood pressure of a small magnitude. Tracheal intubation, however, was associated with increases in both heart rate and arterial pressure which were significant for one minute after intubation. The peak increases in heart rate and blood pressure were 23% and 11% respectively during a normal sequence induction, and 26% and 10% during a rapid sequence induction.

Average time between administration of vecuronium and thiopentone in the rapid sequence induction group was 38 seconds (range 22–50 seconds). Intubation in the normal induction sequence group was performed 3 minutes after vecuronium administration and after 80–90 seconds in the rapid sequence induction group. Intubation conditions were clinically acceptable in all patients. Onset and duration of clinical relaxation were determined using a Myotest and were described as the time from relaxant administration to disappearance and re-appearance respectively of all four responses to train-of-four stimulation. These are shown in Table 4 and were clearly dose-related. Both induction techniques were deemed acceptable by all patients when questioned on the day after operation.

Discussion

Good control of IOP during intra-ocular surgery is normally attained with controlled ventilation facilitated by the use of non-depolarising muscle relaxants. Agents such as tubocurarine, pancuronium, alcuronium or atracurium, given during steady state anaesthesia, either reduce or produce no change in intra-ocular pressure.[9–12] However, it is well known that administration of many of these relaxants results in increase in heart rate or decrease in blood pressure, and other clinical signs of histamine liberation. This is particularly the case when they are used in relatively large doses which, in addition, result in prolonged neuromuscular block, as has been shown with pancuronium.[2] Vecuronium offers several well-documented advantages, such as cardiovascular stability and relatively shorter duration of action, even when administered in relatively large doses.[3,13] Reports by Sia and Rashkovsky[6] and Vilardi *et al.*[7] suggested that vecuronium was suitable for intra-ocular surgery but these workers did not report IOP changes with this relaxant under steady state anaesthesia. In fact, Sia and Rashkovsky[6] did not measure IOP until after intubation. The present study has shown that, under steady state anaesthesia and controlled ventilation, administration of vecuronium produces a significant reduction in IOP. These results are similar to those reported recently by Jantzen and co-workers,[8] who explained this decrease as due to a decrease in central venous pressure. It is also clear that vecuronium administration during steady state anaesthesia results in no change in heart rate or blood pressure.

Use of vecuronium as part of a normal sequence induction has also been associated with good stability of IOP. Use of thiopentone obviously produces a great beneficial effect and is well known. Intubation produces an increase in IOP but it is still below the control levels and rapidly decreases as the effect of this stimulus passes off.

Of greater interest is the use of vecuronium as part of a rapid sequence induction where the use of suxamethonium is contraindicated and associated with an increase in IOP above the control values.[12] The present study shows that vecuronium, when used as part of this technique in a somewhat larger dose of 0.15 mg/kg, does not increase the IOP above control values at any time. A recent report[14] suggested that both vecuronium and atracurium are unsuitable for this purpose because the IOP is increased during induction, and that intubation conditions are not always good. The difference lies in our use of a larger dose of vecuronium in rapid sequence induction, since it has been shown previously that intubation conditions and onset of neuromuscular block are improved if the dose of vecuronium is increased from 0.1 to 0.15 mg/kg, yet the duration of clinical relaxation is still only about 45 minutes.[3,15] This is also the result in the present study (Table 4) as concerns the onset of neuromuscular block and the observation that intubation conditions were acceptable in all patients. The dose of vecuronium was not increased beyond 0.15 mg/kg since that results only in a block of longer duration, without improvement either in the onset of action or in intubation conditions.[3] It is also clear from Table 3 that heart rate and blood pressure changes when 0.1 and 0.15 mg/kg vecuronium are used in a normal sequence or rapid sequence induction technique, respectively, are well within acceptable limits of these induction techniques. Atracurium could also be used in this situation but its use in larger doses may occasionally give rise to significant histamine liberation.

The ages of the patients in the three groups were not similar but this is unlikely to have had any influence on the IOP results, since baseline IOPs were similar in the three groups irrespective of age.

In conclusion, vecuronium administration in a dose of 0.1 mg/kg was associated with a significant decrease in IOP during steady state anaesthesia. Its use as part of a normal sequence induction, in a dose of 0.1 mg/kg, was not associated with an increase in IOP above control values. Vecuronium 0.15 mg/kg produced acceptable intubation conditions in all patients when used in a rapid sequence induction technique; this makes it suitable for use in this induction technique. Intubation increased IOP in both groups compared to values immediately before intubation but IOP never exceeded the control (awake) values.

Acknowledgments

We thank the nursing and other staff of the eye operating theatres at the Royal Victoria Hospital, Belfast for their cooperation.

References

1. Morrison JD, Mirakhur RK, Craig HJL. *Anaesthesia for eye, ear, nose and throat surgery*, 2nd edn. London/Edinburgh: Churchill-Livingstone: 1985: 151–64.
2. Brown EM, Krishnaprasad D, Smiler BG. Pancuronium for rapid induction technique for tracheal intubation. *Canadian Anaesthetists' Society Journal* 1979; **26:** 489–91.
3. Mirakhur RK, Ferres CJ, Clarke RSJ, Bali IM, Dundee JW. Clinical evaluation of Org NC45. *British Journal of Anaesthesia* 1983; **55:** 119–24.
4. Robertson EN, Booij LHDJ, Fragen RJ, Crul JF. Clinical comparison of atracurium and vecuronium (Org NC45). *British Journal of Anaesthesia* 1983; **55:** 125–9.
5. Baird WLM, Savage DS. Vecuronium—the first years. In: Norman J, ed. *Clinics in anaesthesiology*. London: W.B. Saunders, 1985: 347–60.
6. Sia RL, Rashkovsky OM. Org NC45 and intraocular pressure during anaesthesia. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 219–21.
7. Vilardi V, Sanfilippo M, Pelaia P, Gasparetto A. The effect of vecuronium on intraocular pressure during general anaesthesia. In: Agoston S, Bowman WC, Miller RD, Viby-Mogensen J, eds. *Clinical Experiences with Norcuron, Symposium, Geneva, 1983. Current Clinical Practice Series 11.* Amsterdam: Excerpta Medica, 1983: 163–6.
8. Jantzen J-P, Hackett GH, Erdmann K, Earnshaw G. Effect of vecuronium on intraocular pressure. *British Journal of Anaesthesia* 1986; **58:** 433–6.
9. Al-Abrak MH, Samuel JR. Effect of general anaesthesia on the intraocular pressure in man: comparison of tubocurarine and pancuronium in nitrous oxide and oxygen. *British Journal of Ophthalmology* 1974; **58:** 806–10.
10. George R, Nursingh HA, Downing JW, Welsh NH. Non-depolarizing neuromuscular blockers and the eye: a study of intraocular pressure. Pancuronium versus alcuronium. *British Journal of Anaesthesia* 1979; **51:** 789–92.
11. Maharaj RJ, Humphrey D, Kaplan N, Kadwa H, Blignaut P, Brock-Utne JG, Welsh N. Effects of atracurium on intraocular pressure. *British Journal of Anaesthesia* 1984; **56:** 459–63.

12. Lavery GG, McGalliard JN, Mirakhur RK, Shepherd WFI. The effects of atracurium on intraocular pressure during steady state anaesthesia and rapid sequence induction: a comparison with succinylcholine. *Canadian Anaesthetists' Society Journal* 1986; **33:** 437–42.
13. Morris RB, Cahalan MK, Miller RD, Wilkinson PS, Quasha AL, Robinson SL. The cardiovascular effects of vecuronium (Org NC45) and pancuronium in patients undergoing coronary artery bypass grafting. *Anesthesiology* 1983; **58:** 438–40.
14. Mallaiah S, Eltringham RJ, Magauran DM. Atracurium and vecuronium in emergency eye surgery. *Anaesthesia* 1986; **41:** 84–5.
15. Casson WR, Jones RM. Vecuronium induced neuromuscular blockade. The effect of increasing dose on speed of onset. *Anaesthesia* 1986; **41:** 354–7.

Anaesthesia, 1987, Volume 42, pages 950–957

Suxamethonium in myasthenia gravis

A. P. WAINWRIGHT AND P. M. BRODRICK

Summary

The effects of suxamethonium 1.0 and 0.5 mg/kg were studied in myasthenic patients. Resistance was not encountered at the 1.0 mg/kg dose but was seen at the lower dose. A non-depolarising type of block developed in patients in both groups. However, recovery from the non-depolarising block was not prolonged beyond the requirements of surgery. The neurophysiological basis for, and clinical implications of these findings are discussed.

Key words

Complications; myasthenia gravis.
Neuromuscular relaxants; suxamethonium.

Myasthenia gravis is a neuromuscular disorder characterised by fatigue and muscle weakness. The failure of neuromuscular transmission and the resulting weakness are associated with both structural and functional defects at the neuromuscular junction. The major defect is due to an anti acetylcholine receptor antibody which increases the rate of breakdown of acetylcholine receptors and thereby decreases acetylcholine receptor density on the postsynaptic membrane of the neuromuscular junction.[1–4]

Suxamethonium, a depolarising neuromuscular blocking agent, has been shown to produce a non-depolarising (or phase II) block at 3–5 mg/kg in normal subjects.[5–7] However, Foldes[8] suggested that myasthenic patients may be resistant to the action of suxamethonium and develop non-depolarising blockade at normal doses. Resistance has been shown to occur with decamethonium, another depolarising muscle relaxant, in myasthenia gravis.[9–11]

This study was undertaken to establish whether there is resistance to the depolarising relaxant suxamethonium and to ascertain the incidence of development of a non-depolarising type of block at doses of 0.5 and 1.0 mg/kg in a series of patients with myasthenia gravis undergoing thymectomy. The onset of the depolarising block was measured to establish whether suxamethonium is a suitable agent for the rapid sequence induction of anaesthesia. Recovery times from both depolarising and non-depolarising blocks were also observed to determine whether suxamethonium is a suitable agent for use in myasthenic patients who require muscle relaxation for surgery.

A.P. Wainwright,* MB, ChB, FFARCS, Registrar, P.M. Brodrick,† MB, BS, FFARCS, Research Fellow, The National Hospital for Nervous Diseases, Queen Square, London WC1.
* Now Senior Registrar, The London Hospital, Whitechapel Road, London E1.
† Now Senior Registrar, The Middlesex Hospital, Mortimer Street, London W1.
Correspondence should be addressed to Dr A.P. Wainwright, The London Hospital, Whitechapel Road, London E1.

0003–2409/87/090950 + 08 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Methods

Patients

Ten myasthenic patients were compared with 10 non-myasthenic controls. Groups A and B were myasthenics undergoing thymectomy via sternotomy and received 1.0 and 0.5 mg/kg of suxamethonium, respectively. Control groups C and D were non-myasthenics undergoing lower lumbar laminectomy who received suxamethonium 1.0 and 0.5 mg/kg, respectively. Studies on the 1.0 mg/kg groups were completed before the other two groups were studied. The control group patients were all ASA grade 1 or 2 and not receiving any medication likely to affect neuromuscular function. There was no statistically significant difference in weight between any of the groups (Mann–Whitney *U* test). However, there was a statistical difference in age between groups B and D who were given 0.5 mg/kg suxamethonium (Mann–Whitney *U* test, $p < 0.05$).

The Osserman classification[12] for each myasthenic patient was noted (Table 1). Anticholinesterase therapy was omitted on the morning of surgery, which is normal practice for thymectomy patients in this hospital.

Anaesthesia

All patients were premedicated with intramuscular papaveretum 0.1–0.2 mg/kg and hyoscine 0.02–0.04 mg/kg, 90 minutes pre-operatively. Patients received intravenous sodium thiopentone 4–7 mg/kg until loss of the eyelash reflex. Local anaesthesia of the nose with topical cocaine 4% prior to induction in the myasthenic group, and with lignocaine spray 4% 1 mg/kg to the larynx and vocal cords after induction in the control group, was followed by nasal and oral tracheal intubation, respectively. A strain-gauge transducer system was applied to the left thumb. After calibration of the system and initial recording of a supramaximal stimulus, suxamethonium was administered intravenously in a dose of 0.5 or 1.0 mg/kg. Anaesthesia was maintained with nitrous oxide in oxygen (2:1) with 0.5% halothane. The patients' lungs were then ventilated with intermittent positive pressure to achieve an end tidal carbon dioxide level of 4–4.6 kPa as measured by an infrared capnometer (Hewlett–Packard, Model 4710A).

Monitoring

Neuromuscular function was monitored by the evoked twitch response to supramaximal ulnar nerve stimulation at the wrist, using a train-of-four (TOF) pattern of stimulation (2 Hz for 2 seconds).[13,14] Adduction of the thumb was recorded via the strain gauge (Statham 9796) and displayed on a chart recorder (W + W 404, Scientific Instruments, Switzerland). The following definitions were used to describe the parameters of neuromuscular blockade: *depolarising block*, reduction in the first twitch in the train (T_1) but without fade or change in the train-of-four (T_4) ratio; *time to optimal intubation conditions*,[15] from time of injection to reduction in T_1 to $<5\%$ of control; *recovery from depolarising block*, time

Table 1. Clinical details of myasthenic patients.

Age (years)	Sex	Osserman classification	Functional vital capacity, pre-operative (litres)	Prednisolone (mg/day)	Anticholinesterase (mg/kg/day)
Group A (1.0 mg/kg)					
13	M	IIA	2.7	20 ad*	—
50	F	IIA	2.5	—	360
22	M	IIB	3.0	—	—
28	M	III	3.3	20 ad*	360†
15	F	III	3.3	—	720
Group B (0.5 mg/kg)					
16	M	IIA	2.3	—	240
19	F	IIB	4.0	10 ad*	†
35	F	IIB	2.5	12.5 ad*	840
47	F	IIA	2.4	50 ad*	720
46	F	IIA	2.2	—	360

* ad, Alternate days.

† Also received oral azathioprine.

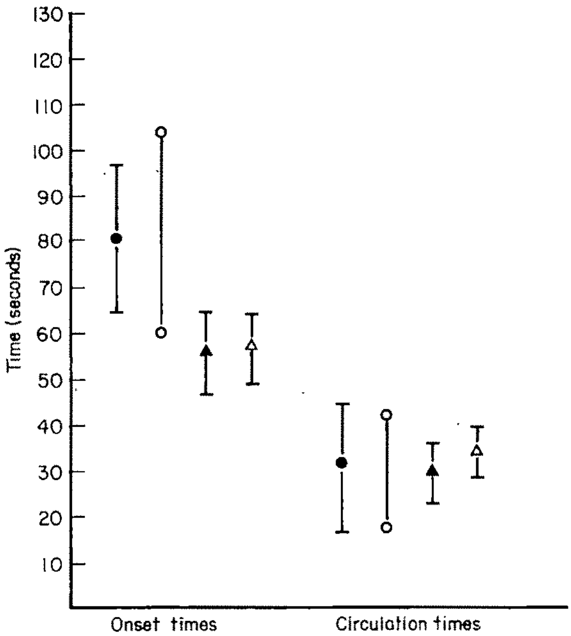


Fig. 1. Onset and circulation times of depolarising block (mean, SEM). ●, Group A ($n = 5$); ○, group B ($n = 2$); ▲, group C ($n = 5$); △, group D ($n = 5$).

from injection to point when T_1 reaches control value again; *resistance to depolarising block*, no reduction of T_1, that is, T_1 remains at control value; *circulation time*,[16] time from injection to first discernible depression of T_1; *non-depolarising block*, reduction in T_1 $>30\%$ of control, with fade; *fade*, any diminution of successive stimuli in the train-of-four; *onset of non-depolarising block*, time from injection to when T_4 reaches <0.8 of T_1, together with reduction of T_1 $>30\%$ of control; *recovery from non-depolarising block*,[17] time from injection to return of T_4 ratio $\geqslant 0.7$, with return of T_1 to control value.

The ECG recording was observed continuously from the time of induction of anaesthesia. The arterial blood pressure was measured using an automated sphygmomanometer (Dinamap 845) on the non-stimulated upper arm. The results were compared using Student's unpaired *t*-test, the Mann–Whitney *U* test and Fisher's exact probability test, as appropriate.

Results

Prior to the administration of suxamethonium all 10 patients in the control groups had a T_4 ratio of 1.0. In six out of the 10 patients with myasthenia gravis the T_4 ratio was also 1.0. The remaining myasthenic patients exhibited a degree of fade, which was considerable in one patient.

Depolarising block

The mean time to onset of depolarising block in the five control patients given suxamethonium 1.0 mg/kg, was 55.6 seconds (SE 8.6, range 34–82). The mean onset time in the five myasthenic patients was 81.2 seconds (SE 15.4, range 54–138) (Figs 1 and 2). The difference was not statistically significant (Mann–Whitney *U* test, $p > 0.05$; unpaired *t*-test, $p = 0.186$).

With the lower dose of suxamethonium, 0.5 mg/kg, the five control patients (group D) developed a depolarising block with a mean onset time of 56.4 seconds (SE 6.9, range 34–76). Of the five myasthenic patients (group B) given this dose, only two developed a depolarising block and the times of onset were 60 and 100 seconds. Three patients were considered to be resistant (Fig. 1). Two patients failed to develop a depolarising block at all (Fig. 3) and a third only

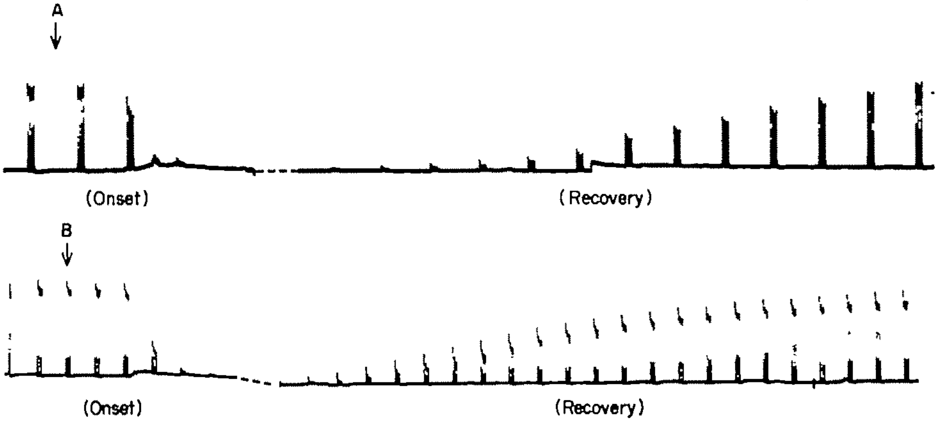


Fig. 2. Control patient who received suxamethonium 1.0 mg/kg (marked A), and myasthenic patient who received suxamethonium 1.0 mg/kg (marked B). This shows a depolarising block and fade on recovery.

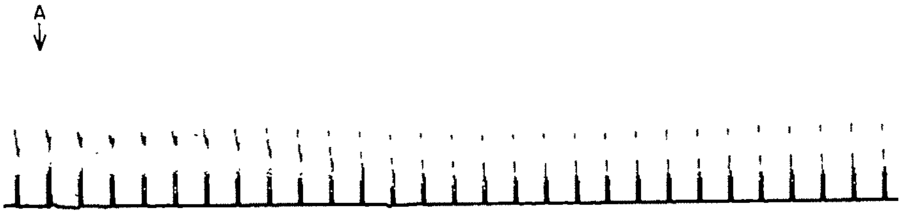


Fig. 3. Myasthenic patient demonstrating resistance to the effect of suxamethonium 0.5 mg/kg (marked A).

developed a 65% reduction in T_1. There was a significant statistical difference from the control group (Mann–Whitney U test, $p < 0.05$).

The mean circulation times in the control groups (C and D) were 30.0 seconds (SE 6.5) and 34.8 seconds (SE 5.8), respectively. In group A, the mean circulation time was 32.4 seconds (SE 14.41). This was not statistically significant when compared to the control groups (Mann–Whitney U test, $p > 0.05$) (Fig. 1).

Recovery from the depolarising block was also longer and more variable in the myasthenic group compared to the control group. The mean recovery time in group A was 22 minutes 19 seconds (SE 12 minutes 15 seconds) and in group B it was 6 minutes 03 seconds (SE 1 minute 53 seconds), compared with the control groups' mean recovery times of 8 minutes 33 seconds (SE 37 seconds) and 8 minutes 09 seconds (SE 37 seconds) (Fig. 4). However, the difference between the myasthenic and control groups did not reach statistical significance (Mann–Whitney U test, $p > 0.05$).

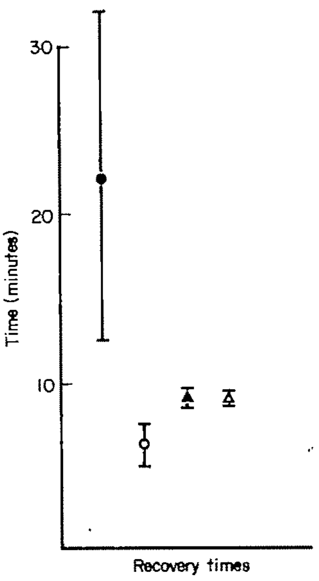


Fig. 4. Recovery times from depolarising block (mean, SEM). ●, Group A (n = 5); ○, group B (n = 2); ▲, group C (n = 5); △, group D (n = 5).

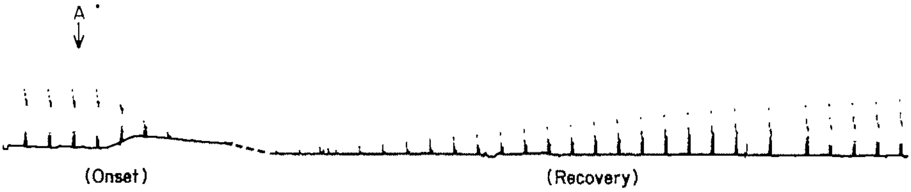


Fig. 5. Myasthenic patient demonstrating a depolarising and a non-depolarising block, who received suxamethonium 1.0 mg/kg (marked A).

Non-depolarising block

No patients in the control groups (C and D) developed a non-depolarising block. Of the five patients in group A, all developed a non-depolarising block (see Fig. 5). This difference was statistically significant for control versus myasthenics (Fisher's exact probability test, $p < 0.05$). The mean time to onset of the non-depolarising block in group A was 7 minutes 01 seconds (SE 4 minutes 50 seconds, range 2 minutes 58 seconds–13 minutes 54 seconds). Mean time to recovery of non-depolarising block was 29 minutes 52 seconds (SE 38 minutes 36 seconds, range 3 minutes 54 seconds–87 minutes 15 seconds). In the five patients in group B, only two developed a non-depolarising block (this was also statistically significantly different from group D; Fisher's test, $p < 0.05$). The onset times were 2 minutes 42 seconds and 3 minutes 54 seconds, and recovery times 18 minutes 24 seconds and 55 minutes, respectively (Fig. 6).

All the remaining patients developed a degree of fade. One patient who was resistant to depolarising block following 0.5 mg/kg of suxamethonium, still developed a non-depolarising block. All patients had recovered from their induced block by the end of surgery. The maximum time to recovery was 87 minutes 15 seconds (Fig. 6). No patient in the myasthenic group required ventilation in the early postoperative period.

One myasthenic patient developed a sinus bradycardia of 50 beats/minute following suxamethonium 0.5 mg/kg. No treatment was given because the blood pressure remained stable throughout.

Discussion

The alterations in response to neuromuscular blocking agents in myasthenia gravis are due to abnormalities in neuromuscular transmission. The end plates are elongated with a widened synaptic cleft but the number and size of the synaptic vesicles of acetylcholine are normal. There is evidence for a pre- and postsynaptic defect at the neuromuscular junction. Anti acetylcholine receptor antibodies, of which there are several types with different binding specificities, attack acetylcholine receptors at both sites.[18] The suggested presynaptic defects are a deficiency in the recycling of immediately available acetylcholine,[19] a defect in the mechanism for replenishing the main presynaptic store of acetylcholine, and interference with the normal receptor ion channel function.[20] Probably of greater importance, is the increased rate of breakdown of postsynaptic acetylcholine receptors by anti acetylcholine receptor antibodies. Alpha-bungarotoxin binding using radioimmunoassay has demonstrated this marked decrease in the density of postsynaptic acetylcholine receptors.[1] Other experimental work[21] has demonstrated lymphocytes in the blood and at the neuromuscular junction sensitised against postsynaptic receptors. Factors in the serum have been found which inhibit alpha-bungarotoxin binding to the receptors.[2] Consequently, in myasthenia gravis a large proportion of end-plate potentials are subthreshold, i.e. they do not trigger an action potential.[22]

Muscle relaxation may be required to facilitate tracheal intubation or produce relaxation for surgical exposure in myasthenic patients who undergo surgery. The time of onset of relaxation is critical in a rapid sequence induction of anaesthesia, and failure to achieve this at the time of attempted intubation may result in vomiting, struggling or failure to intubate at all. It has been shown that 95% depression of T_1 is required for good intubation conditions[15] and, therefore, suxamethonium is usually the drug of choice, as the onset time is short.[16] At 1 mg/kg, good

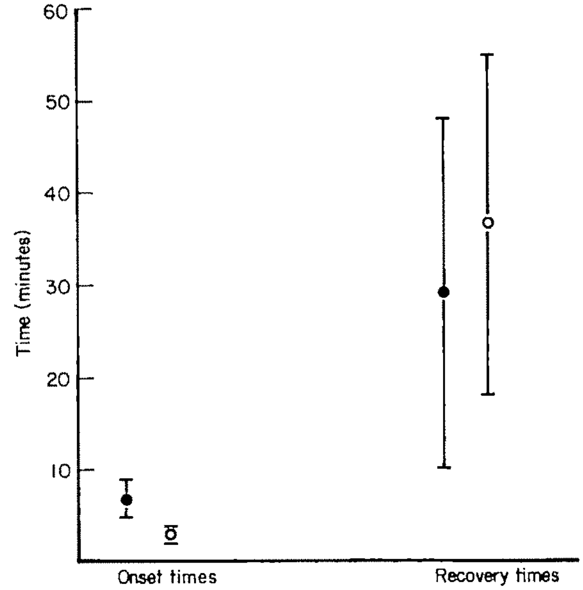


Fig. 6. Onset and recovery times from non-depolarising block (mean, SEM). ●, Group A ($n = 5$); ○, group B ($n = 2$).

intubation conditions are reliably achieved in one arm-to-muscle circulation time.

Suxamethonium produced 95% depression of T_1 in all myasthenic patients given 1 mg/kg, with a mean time of onset of 81.2 seconds (SE 15.4, range 54–138). The longer onset of the depolarising block compared with the control group onset time, 55.6 seconds (SE 8.6, range 34–82), was not due to any difference in circulation time between the two groups. It was noted that the most severely affected myasthenic patient in this group had the longest onset time.

The two new neuromuscular blocking agents, atracurium and vecuronium, can be used in reduced dosage for muscle relaxation in myasthenia gravis[23–25] but are unsuitable when rapid intubation is required, as has previously been shown with other non-depolarising agents.[24] In previous studies intubation was performed at 90 seconds without difficulty, possibly under the effect of thiopentone which provides jaw relaxation.

Earlier work by Churchill-Davidson and Richardson[9,10] which used 2.5–3.0 mg decamethonium, reported resistance to depolarising block in myasthenic patients which was most obvious in the uninvolved muscles of those patients with only ocular weakness. Resistance did not occur in any myasthenic patient in the 1 mg/kg suxamethonium group in our study, although one patient had mainly ocular myasthenia. However, resistance did occur in three patients given 0.5 mg/kg. The mechanism of resistance is unknown but possible explanations could be a change in affinity for suxamethonium or, less probably, the reduced number of receptors available. The resistance to the depolarising block at the lower dosage (0.5 mg/kg) and the wider range of onset time (54–138 seconds) at higher dosage, may make suxamethonium an unsuitable drug for rapid sequence induction of anaesthesia in patients with myasthenia gravis. However, the onset time is still shorter than for the non-depolarising agents.[23,24] Perhaps, the use of a higher dosage may resolve the problem of depolarising block but could lead to an increase in the incidence of non-depolarising block. A non-depolarising block due to suxamethonium has been described in normal subjects and was found to be dose- and not time-dependent,[6] with an abrupt onset at increased dosages of 3–5 mg/kg.[7] The non-depolarising block was suggested to result from the persistence of suxamethonium in an inactive form which combines with the receptor protein and thereby elevates the excitation threshold.[9] However, this block may be due to a presynaptic effect of suxamethonium revealed at lower dosage by the reduced 'margin of safety' in myasthenic patients. Baraka[26] suggested that the loss of available receptors on the postsynaptic membrane explains the resistance and non-depolarising block with suxamethonium, but did not give any supporting data. The clinical significance of a non-depolarising block under these circumstances is unknown. One patient had marked fade with a reduction in the train-of-four ratio to 0.7 prior to the administration of suxamethonium, with no clinical effects on respiration (pre-operative vital capacity 2.5 litres). Fade was seen in four patients prior to the administration of suxamethonium; this was reported in a previous study.[23] Using pancuronium and related drugs, fade is usually more pronounced during recovery from the block than during development, but this may be because of the faster speed of onset than recovery. Fade may be due to blockade of prejunctional receptors or ion channels, which impairs the mobilisation of available acetylcholine stores. The demands of high frequency stimulation mean that the release of acetylcholine cannot meet requirements.[17,27]

All the patients undergoing thymectomy had recovered from the block at the end of surgery, as determined by T_1 and the train-of-four ratio, and none required immediate postoperative ventilation. The longest time to recovery was 87 minutes 15 seconds and this was in the most severely affected patient in the 1 mg/kg group.

Some methods of treatment for myasthenia gravis may affect neuromuscular transmission and thus modify the effects of depolarising agents. Oral pyridostigmine is the most widely used anticholinesterase drug in myasthenia gravis and seven of our patients were receiving this medication. Its effect begins within 10–30 minutes, reaches a peak at about 2 hours and lasts approximately 4 hours,[28] but with continued therapy its effects may accumulate. In all seven of our patients the drug was discontinued at least 8 hours prior to anaesthesia, but it remains unknown whether pyridostigmine had a significant effect on the action of suxamethonium in these cases.

The therapeutic effect of steroids is due to immunosuppression but steroids also have a direct effect on neuromuscular transmission, on the one hand by facilitating spontaneous release of acetylcholine and, on the other, by decreasing MEPP (micro end-plate potential) amplitude.[29] Azathioprine has been shown to prolong the action of non-depolarising muscle relaxants but there is no evidence for a similar effect with suxamethonium.[30]

Plasma exchange is used for the treatment of auto-immune disorders including myasthenia gravis.[31,32] Prolongation of the action of suxamethonium occurs following plasma exchange, when the plasma cholinesterase concentration is less than 20% of normal.[33] A single 4-litre plasma exchange can remove about 64% of plasma cholinesterase[34] and repeated daily plasma exchange virtually removes the enzyme.[35] None of the patients with myasthenia gravis in this study received plasma exchange prior to surgery, although it is currently used as treatment for severe cases of myasthenia gravis in this hospital.

In conclusion, the use of suxamethonium in myasthenia gravis will produce a depolarising block at normal intubation doses (1 mg/kg) with good intubation conditions, although the onset time may be slightly prolonged. It can still be regarded as a suitable agent for rapid sequence induction of anaesthesia for patients with myasthenia gravis. Resistance to a depolarising block can be demonstrated at lower doses (0.5 mg/kg). A non-depolarising block occurs at 1.0 mg/kg but this may not be a significant problem if appropriate monitoring of the degree of block is used.

References

1. Fambrough DM, Drachman DB, Satyamurti S. Neuromuscular junction in myasthenia gravis: decreased acetylcholine receptors. *Science* 1973; **182:** 293–5.
2. Bender AN, Ringel SP, Engel WK, Daniels MP, Vogel Z. Myasthenia gravis: a serum factor blocking acetylcholine receptors of the human neuromuscular junction. *Lancet* 1975; **1:** 607–9.
3. Newsom Davis J. Myasthenia. *British Journal of Hospital Medicine* 1974; **11:** 933–40.
4. Drachman DB. Myasthenia gravis. *New England Journal of Medicine* 1978; **298:** 186–93.
5. Churchill-Davidson HC, Christie TH, Wise RP. Dual neuromuscular block in man. *Anesthesiology* 1960; **21:** 144–9.
6. Katz RL, Wolf CE, Papper EM. The non-depolarising neuromuscular blocking action of succinylcholine in man. *Anesthesiology* 1963; **24:** 784–9.
7. Lee C. Dose relationships of phase II, tachyphylaxis and train-of-four fade in suxamethonium-induced dual neuromuscular block in man. *British Journal of Anaesthesia* 1975; **47:** 841–5.

8. Foldes FF, McNall PG. Myasthenia gravis: a guide for anesthesiologists. *Anesthesiology* 1962; **23:** 837–72.
9. Churchill-Davidson HC, Richardson AT. Neuromuscular transmission in myasthenia gravis. *Journal of Physiology* 1953; **122:** 252–63.
10. Churchill-Davidson HC, Richardson AT. Decamethonium iodide (C10): some observations on its action using electromyography. *Proceedings of the Royal Society of Medicine* 1952; **45:** 179–85.
11. Churchill-Davidson HC, Richardson AT. Neuromuscular transmission in myasthenia gravis. *American Journal of Medicine* 1955; **19:** 691–2.
12. Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. *Mount Sinai Journal of Medicine* 1971; **38:** 497–537.
13. Ali HH, Utting JE, Gray C. Stimulus frequency in the detection of neuromuscular block in humans. *British Journal of Anaesthesia* 1970; **42:** 967–78.
14. Katz RL. Comparison of electrical and mechanical recording of spontaneous and evoked muscle activity. *Anesthesiology* 1965; **26:** 204–11.
15. Harrison GA, Junius F. The effect of circulation time on the neuromuscular action of suxamethonium. *Anaesthesia and Intensive Care* 1972; **1:** 33–40.
16. Minsaas B, Stovner J. Artery-to-muscle onset time for neuromuscular blocking drugs. *British Journal of Anaesthesia* 1980; **52:** 403–7.
17. Jones RM. Neuromuscular transmission and its blockade. *Anaesthesia* 1985; **40:** 964–76.
18. Vincent A, Newsom Davis J. Alpha bungarotoxin and anti-acetylcholine receptor antibody binding to the human acetylcholine receptor. In: Ceccarelli B, Clementi F, eds. *Advances in pharmacology, Vol. 3.* New York: Raven Press, 1979: 269–78.
19. Cull-Candy SG, Miledi R, Trautmann A, Uchitel OD. On the release of transmitter at normal, myasthenia gravis and myasthenic syndrome affected human end-plates. *Journal of Physiology* 1980; **299:** 621–38.
20. Johnson BR, Kim YI, Sanders DB. Neuromuscular blocking properties of suxamethonium and decamethonium in normal and myasthenic rat muscle. *Journal of Neurological Sciences* 1983; **59:** 431–40.
21. Bergmans J, Fannes-Breselow C, Gribomont B. A reassessment of the neurophysiological evidence for a presynaptic defect in myasthenia gravis. *Electromyography and Clinical Neurophysiology* 1976; **16:** 337–51.
22. Baraka A, Afifi A, Muallem M, Kachachi T, Frayah F. Neuromuscular effects of halothane, suxamethonium and tubocurarine in a myasthenic undergoing thymectomy. *British Journal of Anaesthesia* 1971; **43:** 91–5.
23. Bell CF, Florence AM, Hunter JM, Jones RS, Utting JE. Atracurium in the myasthenic patient. *Anaesthesia* 1984; **39:** 691–8.
24. Hunter JM, Bell CF, Florence AM, Jones RS, Utting JE. Vecuronium in the myasthenic patient. *Anaesthesia* 1985; **40:** 848–53.
25. Eisenkraft JB, Sawhney RK, Papatestas AE. Vecuronium in the myasthenic patient. *Anaesthesia* 1986; **41:** 666–7.
26. Baraka A, Dajani A. Atracurium in myasthenics undergoing thymectomy. *Anesthesia and Analgesia* 1984; **63:** 1127–30.
27. Bowman WC. Prejunctional and postjunctional cholinoceptors at the neuromuscular junction. *Anesthesia and Analgesia* 1980; **59:** 935–43.
28. Flacke W. Treatment of myasthenia gravis. *New England Journal of Medicine* 1973; **288:** 27–31.
29. Wilson RW, Dearing Ward M, Johns TR. Corticosteroids: a direct effect at the neuromuscular junction. *Neurology* 1974; **24:** 1091–5.
30. Vetten KB. Immunosuppressive therapy and anaesthesia. *South African Medical Journal* 1973; **47:** 767–70.
31. Pinching AJ, Peters DK, Newsom Davis J. Remission of myasthenia gravis following plasma-exchange. *Lancet* 1976; **2:** 1373–6.
32. Dau PC, Lindstrom JM, Cassel CK, Denys EH, Shev EE, Spitler LE. Plasmapheresis and immunosuppressive drug therapy in myasthenia gravis. *New England Journal of Medicine* 1977; **297:** 1134–40.
33. Lumley J. Prolongation of suxamethonium following plasma exchange. *British Journal of Anaesthesia* 1980; **52:** 1149–50.
34. Wood GJ, Hall GM. Plasmapheresis and plasma cholinesterase. *British Journal of Anaesthesia* 1978; **50:** 945–9.
35. Paterson JL, Walsh ES, Hall GM. Progressive depletion of plasma cholinesterase during daily plasma exchange. *British Medical Journal* 1979; **2:** 580.

Anaesthesia, 1987, Volume 42, pages 958–961

Intercostal catheterisation

An alternative approach to the paravertebral space

A. MOWBRAY, K. K. S. WONG AND J. M. MURRAY

Summary

Twenty-one patients scheduled to undergo thoracotomy or median sternotomy had intercostal catheters inserted pre-operatively. During thoracotomy, under direct vision, the spread of 20 ml of a solution containing bupivacaine and methylene blue was followed. In most cases the spread involved one or two intercostal spaces. However, in all but one patient, dye spread medially to the paravertebral space where it then spread in both caudad and cephalad directions to reach between two and five vertebrae. In three cases, dye was seen crossing the anterior surface of the vertebrae to reach the contralateral aspect. It is concluded that a major component of dermatomal block during intercostal catheterisations may be secondary to paravertebral spread.

Key words

Anaesthetic techniques, regional; intercostal block.

Intercostal nerve block is a technique which has enjoyed great popularity for more than 50 years and, as classically described, involves individual block of each nerve. Recently, conflicting reports of the spread of small volumes of dye in the intercostal space have been published;[1,2] one study showed a wide spread after injection of 3 ml which involved four intercostal spaces, while the second refuted this. However, after the description of subpleural tracking of dye,[1] reports were published of the clinical efficacy of injection of large volumes of local anaesthetic into one intercostal space through an indwelling catheter. In some instances this produced a block of four or more intercostal nerves.[3–6] The pattern of pinprick analgesia in these studies varied from none[4] to block of almost all intercostal nerves,[5] despite injection of similar volumes of local anaesthetic. The proposed modes of spread were epidural,[5] subpleural,[7] paravertebral[6] or a combination of the latter two.[6,7]

The present study was designed to evaluate the extent of spread of a large volume of local anaesthetic injected into the intercostal space in patients undergoing thoracotomy and in whom the spread could be directly visualised.

Methods

Twenty-one patients scheduled for elective thoracotomy or median sternotomy were studied. They consisted of 13 males, age range 16–67

A. Mowbray, BSc, MB, ChB, FFARCS, Visiting Lecturer, K.K.S. Wong, MB, BS, FRCS, Lecturer in Surgery, J.M. Murray, MB, BCh, BAO, FFARCS (I), Visiting Lecturer, Departments of Anaesthesia and Surgery, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong.

Correspondence should be addressed to Dr A. Mowbray, Department of Anaesthesia, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh, Scotland.

0003–2409/87/090958 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

years and weight 42–71 kg, and eight females, age range 25–68 years and weight 35–73 kg. Twenty-two intercostal catheters were inserted, of which 21 were introduced at the angle of the seventh rib and one under the seventh rib in the mid-axillary line.

The first 19 catheters were inserted after the induction of anaesthesia, the last three before induction. All patients received premedication with diazepam and a standard anaesthetic sequence of thiopentone, suxamethonium and tracheal intubation, with maintenance of anaesthesia with oxygen, nitrous oxide, morphine and enflurane. Alcuronium was used to maintain relaxation. Patients had intra-arterial blood pressure monitoring and continuous electrocardiogram (ECG) display throughout surgery.

Intercostal catheterisation was carried out with the patient in the appropriate lateral position for surgery. Under aseptic conditions a 16-gauge Tuohy needle was inserted at the angle of the rib. It was found easier to insert the catheter if the needle was not perpendicular to the chest wall but made an angle of 60° with it, pointing medially. When the needle made contact with the seventh rib it was walked off the inferior surface into the intercostal space and advanced 4 mm. The stylet was removed and, with the bevel facing medially, a 16-gauge epidural catheter advanced as far as possible. Only in three patients was it possible to advance the tip of the catheter more than 2–3 cm into the space.

After careful removal of the Tuohy needle the catheter was secured in place using a transparent dressing and the patient was repositioned, where appropriate, for median sternotomy. Thoracotomy or sternotomy proceeded in the normal fashion until the pleura was opened. At this stage, the lung was gently retracted and the catheter site visualised while the parietal pleura was disturbed as little as possible. In the first five successful cases, 20 ml of a solution which contained 19 ml plain bupivacaine 0.25% and 1 ml methylene blue 1% was injected through the catheter in two 10-ml aliquots 5 minutes apart. The next four successful cases received 20 ml of this solution as a bolus.

Catheters were inserted into the last three patients under local anaesthesia before induction, and in these a modified catheter with a single end hole was inserted. These patients were seated during catheterisation and remained seated for 15 minutes following injection of 20 ml of methylene blue/bupivacaine solution. Analgesia to pinprick was assessed 15 minutes later, before anaesthesia was induced in the standard manner.

In all patients spread of dye was determined in terms of the number of intercostal and paravertebral spaces discoloured. All catheters were removed immediately after surgery.

Results

Twenty-one patients had 22 intercostal catheters inserted; one patient who underwent median sternotomy had bilateral catheterisation. Of these, 12 were technically successful and the spread of dye could be visualised. In 10 patients (Table 1) the dye was not deposited in the correct tissue plane or, for surgical reasons, could not be seen.

The results of injection of dye in the first nine successful catheterisations can be seen in Table 2. The last three patients had pre-operative analgesic levels to pinprick and dye spread over three to four dermatomes (Table 3).

Table 1. Intercostal catheterisations: reasons for failure.

Cause of failure	Number of patients
Pleural adhesions	2
Intrapleural catheter	3
Subcutaneous/intramuscular dye	5

Table 2. Dye spread following 10- and 20-ml injections into intercostal space.

Patient		Number of intercostal spaces	Number of paravertebral spaces
1	10 ml	2	2
	20 ml	2	4
2	10 ml	1	3
	20 ml	3	3
3	10 ml	1	3
	20 ml	2	5
4	10 ml	1	3
	20 ml	1	3
5	10 ml	1	2
	20 ml	1	2
6	20 ml	1	3
7	20 ml	2	3
8*	20 ml	1	0
9	20 ml	1	3

* In this patient the catheter was inserted under the seventh rib in the mid-axillary line.

Table 3. Analgesic levels and dye spread.

Patient	Level of pinprick analgesia	Number of intercostal spaces	Number of paravertebral spaces
10	T_7, T_8, T_9	2	3
11	T_6, T_7, T_8, T_9	1	3
12	T_6, T_7, T_8	1	3

Discussion

There has been a great deal of debate during the last 6 years over the fate of solutions injected into the intercostal space. Spread may be confined to that space,[2] track cephalad and caudad subpleurally,[1,7] enter the paravertebral space[6] or even the epidural space.[5] Analgesia has been produced in some cases with associated loss of pinprick sensation[3,5,7] and, in others, without.[4] In this study, analgesia was significantly associated with spread of dye to the paravertebral space. While the dye could only actually be seen under the parietal pleura and advancing anteromedially under the fascia which covers the anterior surface of thoracic vertebrae, because of the pattern of spread and associated analgesia in patients 10, 11 and 12 it is inferred that the solution also extended medially into the paravertebral space to produce block of the nerves at that level. As in a previous study,[6] spread was typically one interspace above and one or two below the space that contained the catheter.

One study in cadavers[2] gave clear evidence that small volumes injected into the intercostal space are confined there, but perhaps the injection of a large volume disrupts the normal anatomy so much that cephalad and caudal spread is possible. However, the contribution to analgesia of intercostal nerve blockade in this technique seems to be minor. The numbers in this study were small but posture did not seem to have any effect on spread. In all but three cases it was found impossible to feed the catheter more than 3 cm into the intercostal space. In these patients 8–10 cm was inserted without difficulty but the catheters were found to be intrapleural when the chest was opened. Clearly, easy catheter insertion in this technique implies that the tip of the Tuohy needle is lying in the wrong tissue plane. Other causes of failure were pleural adhesions in two patients (in whom it was not possible to know whether or not the catheter was in the correct position), and subcutaneous/intramuscular spread of dye in five. This high rate of displacement (23%), greater than that seen in similar studies,[6,7] was probably due to a combination of short segment of catheter in the intercostal space and traction on subcutaneous tissues and skin by the surgeon during thoracotomy.

In three patients dye spread over the anterior surface of the vertebrae to reach the contralateral side and this may provide the explanation for the epidural spread described in a previous case report.[5] In that particular patient, spread of local anaesthetic was followed using a two-dimensional anteroposterior radio-isotope scan and showed medial spread from the intercostal space apparently into the epidural space. Our study, in three dimensions, clearly shows medial spread anterior to the vertebrae and, while epidural spread cannot be disproved, the lack of cardiovascular effects in the case reported makes our explanation more feasible.

In four out of nine patients with lateral hole catheters there was spread to involve more than one intercostal space and this was also apparent in one of three patients with an end hole catheter. Since the main contribution to analgesia arises from paravertebral spread and not intercostal, it would seem more efficient to encourage medial spread by using an end hole catheter. Patient 8 had a catheter inserted in the midaxillary line and only one intercostal space was involved; therefore this site cannot be recommended for intercostal catheterisation. In this study the injection of 20 ml bupivacaine solution into the intercostal space was very safe. There was no incidence of intravascular injection and no significant haemodynamic changes were seen in any patient.

The spread of 10 ml of injectate was two to three paravertebral spaces and for 20 ml, was two to five; thus, to limit the amount of local anaesthetic used, it may be possible to achieve good spread with less than 20 ml. However, two intercostal catheters inserted three ribs apart would seem to be necessary in order to provide sufficient dermatomal block for thoracotomy. This technique requires further evaluation.

Acknowledgments

We thank Prof. J. A. Thornton for his advice during the preparation of this paper and Miss

B. Li and Miss T. Wong, secretaries to the Department of Anaesthesia, for typing the manuscript.

References

1. Nunn JF, Slavin G. Posterior intercostal nerve block for pain relief after cholecystectomy. Anatomical basis and efficacy. *British Journal of Anaesthesia* 1980; **52:** 253–9.
2. Moore DC. Intercostal nerve block: spread of India ink injected to the rib's costal groove. *British Journal of Anaesthesia* 1981; **53:** 325–9.
3. O'Kelly E, Garry B. Continuous pain relief for multiple fractured ribs. *British Journal of Anaesthesia* 1981; **53:** 989–91.
4. Murphy DF. Continuous intercostal nerve blockade for pain relief following cholecystectomy. *British Journal of Anaesthesia* 1983; **55:** 521–4.
5. Middaugh RE, Menk EJ, Reynolds WJ, Bauman JM, Cawthon MA, Hartshorne MF. Epidural block using large volumes of local anesthetic solutions for intercostal nerve block. *Anesthesiology* 1985; **63:** 214–6.
6. Hosie HE, Crossley AWA. A radiographic study of intercostal nerve blockade in healthy volunteers. *British Journal of Anaesthesia* 1986; **58:** 129–30.
7. Murphy DF. Continuous intercostal nerve blockade. An anatomical study to elucidate its mode of action. *British Journal of Anaesthesia* 1984; **56:** 627–9.

Anaesthesia, 1987, Volume 42, pages 962–964

CASE REPORT

A red patient: immunological reaction to glycine?

P. E. MOSKOVITS, P. RICHES AND N. SONI

Summary

A case of immunological adverse reaction to the commonly used bladder irrigation fluid, glycine, is reported, with discussion of the immunological investigations and possible significance of the results.

Key words

Immune response.

Glycine is commonly used as an irrigation fluid during urological procedures. The complication of water intoxication is well recognised.[1–4] In addition, visual disturbances[5] and hyperammonaemia[6] have been reported. The latter may have resulted from abnormal glycine metabolism due to partial deficiency of arginosuccinate synthetase. When a patient collapsed with an apparent anaphylactic reaction during cystoscopy, a routine immunological screen was performed and yielded some unexpected results.

Case history

A 76-year-old Caucasian male presented for repeat cystoscopy and urethrotomy. Transitional cell carcinoma of the bladder had been diagnosed in 1980 and treated with diathermy on that occasion. Twenty-three further cystoscopies were performed and the last recurrence noted in January 1984. His general health was good and the only finding of note on admission was mild hypertension, adequately controlled by bendrofluazide and a beta-adrenoreceptor blocker.

Premedication consisted of papaveretum 10 mg and atropine 0.6 mg intramuscularly. Anaesthesia was induced with thiopentone 250 mg and he was allowed to breathe spontaneously nitrous oxide–oxygen and halothane via a Magill system. Shortly after induction and during cystoscopy he had a mild bradycardia of 50 beats/minute, which was treated with atropine 0.6 mg. The remaining anaesthetic was uneventful and he was returned to the recovery ward in a satisfactory condition.

His observations were stable on arrival but, several minutes later, he collapsed. It was initially felt he had a primary respiratory problem and it was noted that he appeared unusually red. At this point recovery staff volunteered that they had noted this on previous occasions. Oedema of his lips and conjunctiva was apparent. Ventilation of the lungs and cardiac massage were commenced and he responded rapidly to atropine, calcium chloride, promethazine and hydro-

---

P.E. Moskovits, MB, BS, FFARCS, DRCOG, Senior Registrar, P. Riches, BTech, PhD, MRCPath, Top Grade Biochemist, N. Soni, MB, BS, FFARCS, Senior Lecturer in Anaesthetics, Westminster Medical School.

Correspondence should be addressed to Dr P.E. Moskovits, 2 Beck Street, North Epping, Sydney, NSW 2121, Australia.

0003–2409/87/090962 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

cortisone. He was transferred to the intensive therapy unit where 3 litres of colloid was infused. His trachea was extubated uneventfully after overnight mechanical ventilation.

Various investigations were carried out immediately following his resuscitation. These showed normal serum sodium, cardiac enzymes, ECG and chest X ray. There was a change in total protein from 73 g/litre pre-operatively to 52 g/litre postresuscitation. Albumin also decreased from 38 g/litre to 25 g/litre but then remained stable throughout further investigations. This is pertinent, since serum albumin influences complement measurement. Immunological investigations performed were complement levels, circulating immune complexes, immunoglobulin screen and intradermal testing (done at a later date). The results of these tests showed evidence that C3 activation had occurred (Table 1). *In vitro* investigation of the patient's plasma challenged with glycine solution (1:1000 dilution) showed C3 conversion (approximately 5–10%) after 30 minutes and 1 hour incubation at 35°C. C3 conversion products were detected by immunofixation and quantified by densitometry.[7]

Table 1. Immunological data for patient in whom reaction occurred, and for six controls.

	Samples 3 hours postoperation		
	C3 (g/litre)	C4 (g/litre)	Albumin (g/litre)
Patient	0.7	0.1	25
Control 1	1.3	0.6	37
Control 2	1.7	0.5	36
Control 3	0.9	0.3	30
Control 4	1.4	0.9	25
Control 5	1.0	0.4	33
Control 6	2.2	1.3	22
Reference range	0.7–1.7	0.1–0.7	30–42

No conversion was seen in the control serum with these agents. There was no evidence of Factor B conversion. No antibodies or circulating immune complexes were detected.

IgE was 74 U/ml, IgG 7.4 g/litre, IgA 2.8 and IgM 1.5 g/litre (analysed by polyethylene-precipitable IgC and C3 conglutinin-binding immunoglobulin). Intradermal testing failed to show any reaction.

Discussion

In approximately only 20% of adverse anaesthetic drug reactions is there a truly allergic mechanism in the sense of immunological memory, and probably many factors play a part in most reactions. It is impracticable to assay histamine levels at the time of the event and tests afterwards are usually too late. In this case, the finding of *in vitro* complement activation by glycine solution was unexpected and difficult to explain. The incidence of *in vitro* complement conversion with glycine is not recorded and, consequently, a pilot study of several patients was carried out to determine whether this is a common finding.

Pilot study

Six patients who had cystoscopic procedures performed with glycine as the irrigation fluid were selected. Four of these patients had been exposed to glycine solution previously. Blood samples were assayed for albumin, C3, C4 and also for *in vitro* complement conversion. There was no evidence of complement conversion *in vivo* or *in vitro* in five of the patients studied. One patient showed a minor increase in complement C3 and C4 levels postoperatively and demonstrated minimal complement conversion *in vitro*, both to glycine and to normal saline. This is not thought by the immunologist to be significant. These negative findings in other patients who had cystoscopies suggest that the *in vitro* activation of complement by glycine in the patient who had a reaction, may be of significance.

A serious adverse reaction occurs in about 1:5000 to 1:10 000 anaesthetics and guidelines for investigation have been suggested.[8] Prompt recognition of the problem and appropriate treatment must improve the management of these patients. This requires an awareness of the potential for adverse reactions and we consider that glycine solution may need to be included in the heterogeneous list of guilty agents just as much as suspected offenders such as Althesin and tubocurarine, and less suspected drugs such as hydrocortisone and methylprednisolone.

Glycine, although not strictly an anaesthetic drug, is important to anaesthetists since its use seems likely to increase with the growth of the geriatric population and urological surgery. We have suggested that our patient's bladder be irrigated with physiological saline, rather than glycine, when he next presents, since check cystoscopy in the absence of abnormal findings requires no electric current. This has also been recommended for ultrasonic stone disintegration during percutaneous ultrasonic lithotripsy following a case of transurethral resection syndrome where glycine was used.[9]

There is no doubt that our patient had an immunological reaction, whatever the cause of collapse. The *in vitro* activation suggests that glycine may have been implicated, although the significance of *in vitro* activation of complement has yet to be established in immunological screening.

Acknowledgments

Our thanks are due to Jo Sheldon for her conscientious and time-consuming laboratory analysis in the Protein Reference Laboratory (Department of Chemical Pathology, Westminster Hospital).

References

1. Thomas D, Hales P. Overhydration during transurethral resection of the prostate using glycine as an irrigating solution. *Anaesthesia and Intensive Care* 1984; **12:** 366–9.
2. Osborn DE, Rao PN, Greene MJ, Barnard RJ. Fluid absorption during transurethral resection. *British Medical Journal* 1980; **281:** 1544–50.
3. Charlton AJ. Cardiac arrest during transurethral prostatectomy after absorption of 1.5% glycine. A case report and review of the literature. *Anaesthesia* 1980; **35:** 804–6.
4. Strode MD. Glycine irrigation. *Anesthesiology* 1973; **39:** 567.
5. Kaiser R, Adragna MG, Weis FR Jr, Williams D. Transient blindness following transurethral resection of the prostate in an achondroplastic dwarf. *Journal of Urology* 1985; **133:** 685–6.
6. Ryder KW, Olson JF, Kahnoski RJ, Karn RC, Oei TO. Hyperammonaemia after transurethral resection of the prostate: a report of 2 cases. *Journal of Urology* 1984; **132:** 995–7.
7. Whicher JT, Higginson J, Riches PG, Radford S. Clinical applications of immunofixation: detection and quantitation of complement activation. *Journal of Clinical Pathology* 1980; **33:** 781–5.
8. Watkins J. Adverse anaesthetic reactions. An update from a proposed national reporting and advisory service. *Anaesthesia* 1985; **40:** 797–800.
9. Laxenaire MC, Moneret-Vautrin DA, Watkins J. Diagnosis of the cause of anaphylactoid anaesthetic reactions. *Report of the Recommendations of the Joint Anaesthetic and Immuno-Allergological Workshop, Nancy, France, 19 March 1982.*

Anaesthesia, 1987, Volume 42, pages 965–974

CASE REPORT

Removal of a giant ovarian cyst

Anaesthetic and intensive care management

P. MORRISON AND G. MORGAN

Summary

Excision of a giant ovarian cyst may be associated with considerable mortality. Problems stem from the size of the cyst and the emaciated state of the patient. We describe a case in which the patient's pre-operative nutritional and psychological state required attention. Gradual pre-operative drainage of a cyst weighing 113 kg was carried out successfully. The main problems intra-operatively stemmed from copious blood loss and the duration of surgery. Postoperatively, ventilatory inadequacy occurred and was probably caused by altered mechanics of ventilation, postoperative pain and pulmonary oedema. We suggest ways in which the management of such cases might be improved.

Key words

Surgery; ovarian cystectomy.

This report describes the gradual pre-operative drainage of 48 litres of fluid and the subsequent excision of an ovarian cyst that weighed 72 kg. Management of such cases is associated with appreciable mortality. In two of eight reports,[1,2] the procedure resulted in the death of the patient; the survivors encountered serious cardiovascular complications.[3–5]

The potential problems associated with removal of a giant ovarian cyst are summarised in Table 1. In the pre-operative period, the psychological and nutritional aspects are of importance. Controversy exists about the benefits of pre-operative cyst drainage.[6] Operative problems include the risks of anaesthesia in such a large patient, blood loss and hypothermia during a long operation. Postoperatively, cardiorespiratory dysfunction may originate from several sources.[1–6] Severe intestinal distension may occur[5] and has led to death.[1] After the available information had been considered, it was decided that the cyst should be drained gradually before operation and that pre- and postoperative care should take place in the intensive therapy unit.

Case history

A 58-year-old female patient was referred after she had become almost totally immobilised by an abdominal tumour which had been enlarging for many years. Previously, she had persistently refused treatment.

Physical examination revealed an emaciated woman with gross abdominal distension and mild oedema of the legs. She weighed 148.7 kg

---

P. Morrison,* MB, BS, Senior House Officer, G. Morgan, FFARCS, Consultant, Intensive Care Unit, Royal Cornwall Hospital, Treliske, Truro, Cornwall.

Correspondence should be addressed to Dr G. Morgan please.

* Present address: P. Morrison, FFARCS, Registrar in Anaesthetics, St Mary's Hospital, Praed Street, London W2.

0003–2409/87/090965 + 10 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Potential problems in the surgical management of a giant ovarian cyst.

Pre-operative	Operative	Postoperative
Psychological fear of hospitals Nutritional anaemia hypoalbuminaemia cachexia pressure sores Mobility size of patient general debility Cardiovascular aortocaval compression Ventilatory distortion of thorax Cyst drainage merits of pre-operative drainage Monitoring biochemical ventilatory cardiovascular haematological	*Cyst drainage* Surgical Anaesthesia for insertion of drains *Resection of cyst* Size of patient position on table Ventilatory dysfunction cardiovascular origin plasma protein levels abnormal mechanics Cardiovascular dysfunction aortocaval compression hypovolaemia blood replacement coagulation Hypothermia Anaesthesia Premedication sedative antacid Induction position acid aspiration choice of drugs Maintenance muscle relaxant ventilation anaesthetic agent Intravenous cannulae Monitoring cardiovascular temperature biochemical Surgical incision, adhesions closure, duration, binder	Cardiovascular dysfunction hypotension hypovolaemia coagulation Ventilatory dysfunction cardiovascular origin plasma protein levels abnormal mechanics elective postoperative IPPV postoperative pain Postoperative pain relief sedation Hypothermia Biochemical Ileus DVT prophylaxis Nutrition Mobilisation

and had an abdominal girth of 170 cm. She was able to stand and walk by shuffling, but only a few steps. She was not dyspnoeic, despite marked flaring of the rib cage. Examination of her cardiovascular system showed no abnormality. Despite her emaciation she had no pressure sores. Haematological and biochemical investigation demonstrated a mild hypochromic microcytic anaemia (Hb 9.4 g/dl) and a serum albumin of 25 g/litre, both suggestive of poor nutritional status (serum albumin normal range 28 ± 2 g/litre). The abdominal swelling was shown to be a giant ovarian cyst.

Pre-operative management

The patient had a profound fear of doctors and hospitals and the clinical team were apprehensive that she might discharge herself before treatment could be completed. She was therefore admitted to a single room in a gynaecological ward, where initial haematological and biochemical investigations were performed. She was visited by the operating theatre and intensive care nursing staff, physiotherapist and dietician. The proposed plan of treatment was explained to her and she was transferred to the intensive therapy unit (ITU).

It was decided to drain the cyst gradually, since it would be impossible to remove it intact. Two tubular drains were inserted in the operating theatre. In preparation for this procedure, the patient was premedicated with an oral antacid (magnesium trisilicate mixture BP 30 ml orally, 30 minutes pre-operatively) as prophylaxis against acid regurgitation. She was transported to the operating theatre in the left lateral position to avoid aortocaval compression. The patient was too large to fit on a single operating table. Therefore, the procedure took place on the patient's bed, which could be tipped head down if required, with the bed head removed.

After pre-oxygenation for 4 minutes with 100% oxygen, anaesthesia was induced with the patient in the left lateral position using etomidate 12 mg intravenously and maintained by spontaneous breathing of nitrous oxide 70%, oxygen 30% and enflurane from a Mapleson A circuit. It was considered reasonably safe to allow this technique for a short period.

During the procedure a 16-gauge central venous catheter was inserted via a right antecubital vein and a 20-gauge cannula placed in the left radial artery for blood pressure measurement and blood sampling. The patient was returned to the ITU.

Cyst drainage took place over a period of 5 days. Ventilatory distress and pulmonary oedema have been reported following drainage of a large ovarian cyst.[3] Therefore, during drainage, central venous pressure (CVP), arterial pressure and pulse rate were monitored continuously. Daily estimations of haemoglobin, urea, electrolytes and serum albumin were made.

A total of 48.4 litres of cyst fluid were allowed to drain, starting at a rate of 300 ml/hour and increasing to 750 ml/hour. On the fourth day, 16.68 litres of cyst fluid drained. Drainage decreased spontaneously on the fifth day and was discontinued because the tumour was now considered to be operable.

During drainage, cardiovascular stability and urine output were maintained by transfusion with human plasma protein fraction (HPPF) or blood. The patient developed a positive fluid balance of almost 8 litres of colloid over this period. Of this, 3.5 litres were HPPF and 2.5 litres, blood. The patient's serum albumin concentration increased from 25 to 29 g/litre and the haemoglobin concentration increased from 9.4 to 12.5 g/dl. Urea and electrolyte levels and blood coagulation remained normal. No signs of pulmonary oedema were noted, either clinically or radiologically.

The patient's only complaint pre-operatively concerned mobility. Drainage of the cyst led to instability of the abdominal mass so that turning in bed became difficult. Pre-operative hypotension due to aortocaval compression did not occur; the patient found the lateral position most comfortable and was discouraged from lying on her back.

Removal of cyst

Prior to surgery, 8 units of blood were ordered and the availability of fresh frozen plasma and platelets was confirmed. The patient was given an oral bowel preparation of neomycin and mannitol in order to sterilise the bowel and reduce its contents to a minimum in case of intra-operative perforation. Attempts to obtain pre-operative ventilatory function tests were unsuccessful because of a malfunction in the machine and inability of the patient to cooperate fully with the tests.

No sedative premedication was prescribed since the patient was by now familiar with the operating theatre personnel. An oral antacid (magnesium trisilicate mixture BP 30 ml) was given 30 minutes pre-operatively as prophylaxis against acid aspiration, as was then the practice prior to Caesarean section at this hospital. The patient was still too large to fit on one operating table and was transferred awake onto two placed side by side. The left lateral position was considered most suitable for anaesthesia and surgery. In addition to the central venous and arterial cannulae still *in situ*, two 14-gauge catheters were inserted into forearm veins for intravenous fluid replacement.

Considerable heat loss was anticipated from the large surface area of the operation site. Precautions taken to avoid hypothermia included provision of a heated water mattress on each operating table. After induction of anaesthesia, the patient's legs, shoulders and arms were covered with aluminium foil blankets secured with adhesive tape. All intravenous fluids were warmed prior to administration. The operating theatre temperature was kept at 24°C and the operating theatre doors were kept closed. Rectal temperature was measured continuously.

After pre-oxygenation for 4 minutes with 100% oxygen, anaesthesia was induced with etomidate 12 mg intravenously. Muscle relaxation for tracheal intubation was provided by suxamethonium 50 mg intravenously. Cricoid pressure was applied just before induction.

Artificial ventilation of the lungs was commenced with nitrous oxide 70% and oxygen 30% through a partial rebreathing system using low

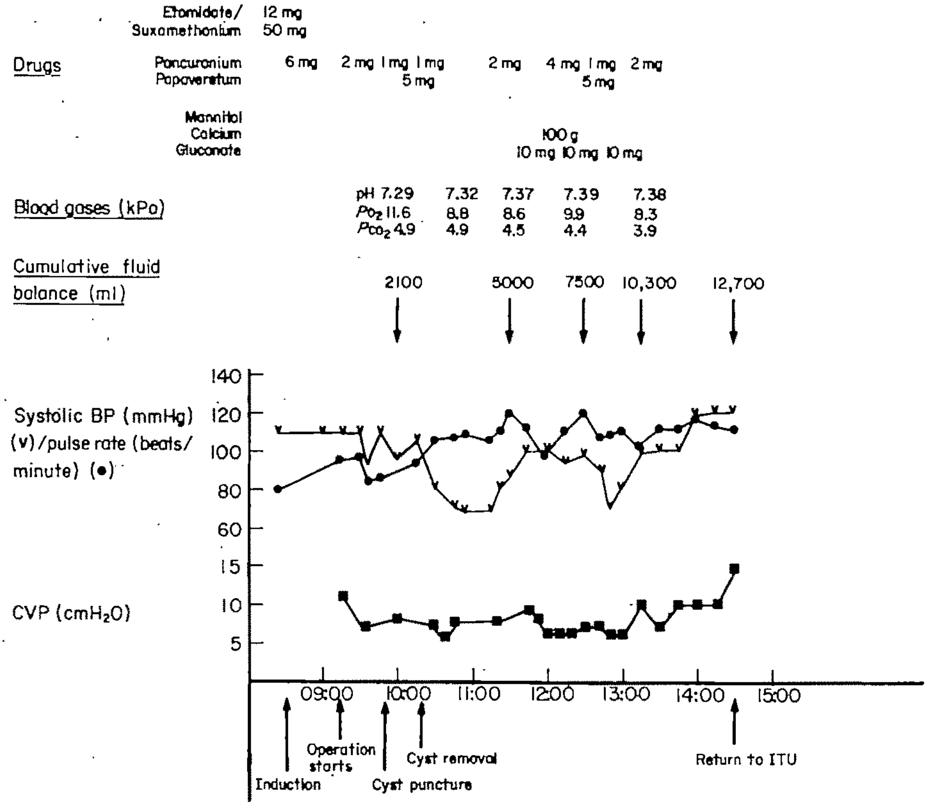


Fig. 1. Excision of giant ovarian cyst: course of anaesthesia.

flow rates and a carbon dioxide absorber. Incremental doses of papaveretum 5 mg and pancuronium 4 mg were administered to provide analgesia and muscle relaxation. These drugs were chosen for their minimal and predictable effects on cardiovascular stability and their suitability for use during postoperative ventilation. A 12-gauge nasogastric tube was passed in anticipation of postoperative ileus.

Pulse rate and direct arterial and central venous pressure traces were displayed continuously. Arterial blood gas measurements were made hourly to assess the adequacy of ventilation and the acid–base status. Blood loss was estimated as accurately as possible by immediate weighing of swabs and measurement of blood aspirated from the operative field. The course of anaesthesia is represented graphically in Fig. 1.

The pulse and blood pressure remained stable until the peritoneal cavity was opened and the cyst punctured. During this time there was considerable blood loss from small vessels resulting from dissection of the cyst from surrounding tissue, and the CVP decreased from 12 to 7 cm H_2O. Copious haemorrhage continued during further dissection and eventual removal of the cyst. After an hour of surgery the patient's arterial pressure began to decrease, and reached a nadir of 70 mmHg after 2 hours. The heart rate increased to 120 beats/minute and subsided only marginally with transfusion. After 5 hours of surgery, when the haemorrhage was brought under control and blood volume restored, the heart rate, arterial pressure and CVP began to return to normal values. Intra-operative blood loss was estimated at 10 litres. A total of 4.4 litres of whole blood, 3.6 litres of HPPF, 3 litres of gelatin solution and 1.7 litres of crystalloid solutions were transfused intra-operatively. After 2 hours of surgery the patient's haemoglobin had decreased to 6 g/dl and a further 8 units of blood were ordered. Mannitol 10% 200 ml was given to maintain renal blood flow and urine production.

Blood gas analysis 1.5 hours after induction of anaesthesia, demonstrated a metabolic acidosis which was not corrected since subsequent values showed considerable improvement. The acidosis was not satisfactorily explained. The arterial oxygen tension decreased gradually during the procedure, from 11.6 to 8.3 kPa, despite institution of 0.5 kPa positive end expiratory pressure (PEEP).

A multilocular mucinous cystadenoma weighing 72 kg was removed which contained 12 litres of dark-brown gelatinous fluid. The duration of surgery was 6 hours, during which the patient's core temperature decreased to 34°C.

The wound was closed with great care using a technique that involved resection of a large quantity of redundant abdominal wall between the rectus muscles to reduce the size of the abdominal cavity.[4] The purpose of this was to reduce the risk of postoperative intestinal distension and also to increase the mechanical advantage of the ventilatory muscles by reducing expansion of the rib cage by elastic recoil. A small pillow was incorporated into an abdominal binder.

Postoperative management

The postoperative course is shown in Fig. 2. The patient was returned to the ITU after surgery, where her condition stabilised over 24 hours. On arrival, her arterial pressure was 125/60 mmHg, heart rate 100 beats/minute and right atrial pressure 7 cm H_2O (measured from the mid-axillary line). Her core temperature was 34°C and she had cool, vasoconstricted limbs.

In the early postoperative period, problems anticipated were those resulting from haemorrhage and prolonged duration of surgery, e.g. hypothermia and an unstable cardiovascular system. Disorders of coagulation were expected after the large transfusion. Other problems anticipated included ventilatory inadequacy as a result of alterations in ventilatory mechanics and postoperative pain. For these reasons the patient's lungs were ventilated artificially until cardiovascular, ventilatory and metabolic stability had been achieved. PEEP 0.5 kPa was added to reduce pulmonary atelectasis. Peak inflation pressures were between 1 and 1.5 kPa. During stabilisation, sedation was provided using intravenous phenoperidine in boluses of 1 mg plus an infusion of between 0 and 5 mg/hour. No muscle relaxants were used. Pain relief was adequate and the patient was conscious and cooperative.

It was planned to restore circulating blood volume and normothermia over the first 12 hours. Colloid solutions comprised a large proportion of the volume replaced because of the risk of formation of interstitial pulmonary oedema. A total of 4.8 litres of blood, 1.6 litres of HPPF and 5.3 litres of crystalloid solutions were administered. Our aim was to maintain systolic arterial pressure greater than 100 mmHg, right atrial pressure 10 cm H_2O and urine output in excess of 40 ml/hour (1 ml/kg/hour estimated postoperative weight). Urine output decreased below 30 ml/hour on two occasions; mannitol 10% 100 ml intravenously was given on each. Chlorpromazine 25 mg intramuscularly and a dopamine infusion (2–5 μg/kg/hour) improved peripheral perfusion and urine output during this period.

Over the first 24 hours, the patient's heart rate decreased from 110 to 80 beats/minute. Systolic arterial pressure was labile and varied between 80 and 120 mmHg, apparently uninfluenced by right atrial pressure. Normothermia was attained within 12 hours of completion of surgery. Arterial blood gas analysis demonstrated normal acid–base balance. Arterial oxygen tension ($Pa\text{O}_2$) remained slightly low for 48 hours postoperatively. A chest X-ray film taken 24 hours postoperatively demonstrated mild pulmonary oedema which resolved over the next day with fluid restriction and frusemide 20 mg intravenously.

Blood coagulation was impaired during the first 24 hours. The platelet count decreased from a pre-operative level of 608 × 10^9/litre to 103 × 10^9/litre. The prothrombin time and activated partial thromboplastin time were 20 (13) and 50 (44) seconds, respectively (controls in parentheses), with normal levels of fibrin degradation products; these findings suggested dilution of clotting factors due to transfusion with factor-free replacement. The impairment was corrected with fresh frozen plasma and platelets, although there was no clinical evidence of abnormal coagulation.

By 48 hours postoperatively, the patient was able to generate tidal volumes of 500 ml and her $Pa\text{O}_2$ was 10 kPa with an inspired oxygen concentration of 30%. In view of her satisfactory clinical condition, her trachea was extubated and 35% oxygen was administered from a fixed

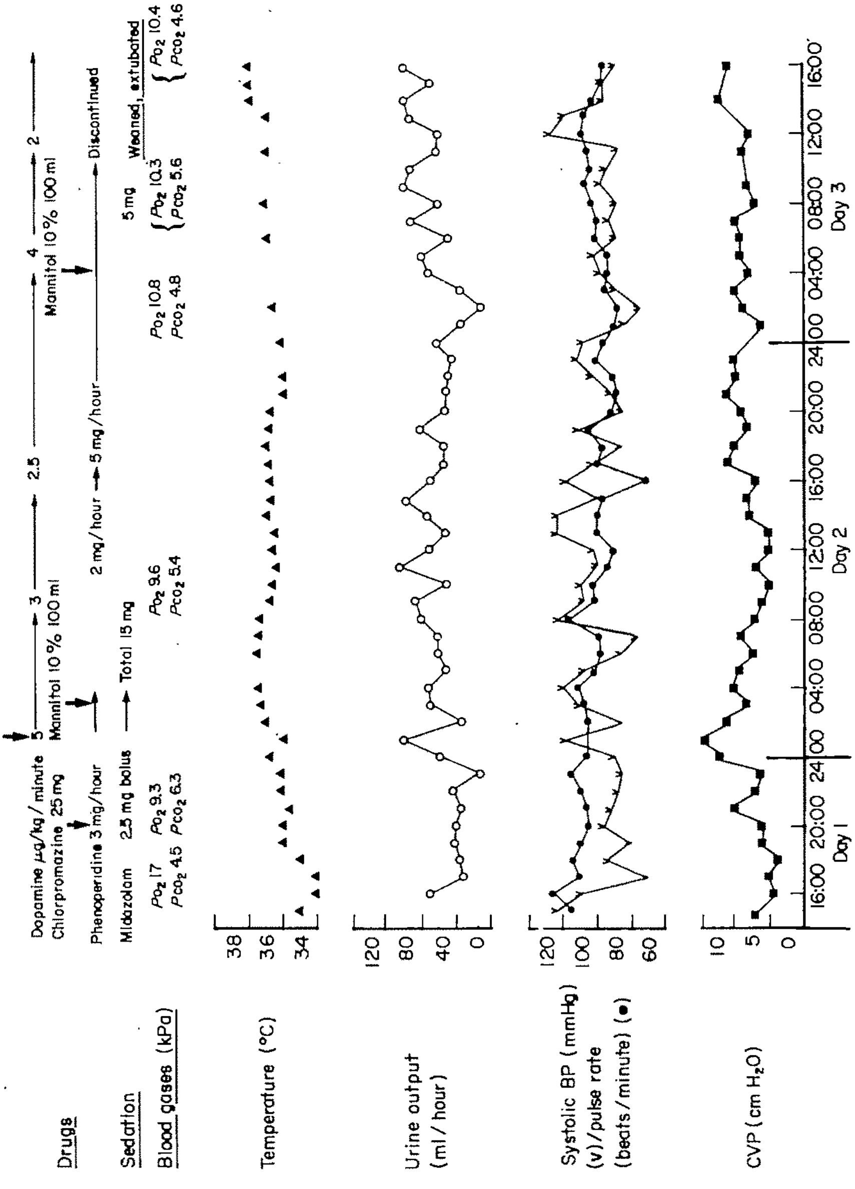


Fig. 2. Excision of giant ovarian cyst: postoperative course.

performance mask. The patient found it difficult to cough immediately following extubation, due to her lax abdominal wall and marked flaring of the rib cage. Tightening of the abdominal binding and provision of analgesia, again using a phenoperidine infusion, resulted in adequate expectoration.

As prophylaxis against thromboembolism, graduated elastic support stockings were worn throughout the postoperative period and Dextran 70 in 5% dextrose 500 ml daily was given from the third to the ninth postoperative day. Parenteral nutrition was started on admission to the ITU and was discontinued after 4 days as the patient progressed to an oral diet. The patient did not develop an ileus or intestinal distension. The patient was able to sit out of bed on the fifth postoperative day and was discharged to a community hospital after 14 days.

Discussion

Patients with a giant ovarian cyst present rarely and in a District General Hospital it is unlikely that clinicians will have previous experience.

Pre-operative management

The patient's psychological state and antipathy towards the idea of hospitalisation and doctors in general, should not be underestimated. Apprehension on the part of the medical team that the patient might discharge herself before her operation, together with her cachectic and debilitated appearance, led to reluctance to pursue aggressive investigation and to the adoption of a simple approach. As a result, less information of possible value was obtained. For example, measurement of pulmonary artery wedge pressure would have defined the aetiology of the pulmonary oedema described during cyst drainage. Persistence with ventilatory function tests might also have been of value.

The patient's nutritional status could have been improved pre-operatively. Her pre-operative weight was 148.7 kg but, after drainage and excision of the cyst, her weight was 35 kg. Her low plasma albumin and iron deficiency both signified poor nutritional status and it is known that surgical mortality is higher in the debilitated patient. A longer period of pre-operative enteral hyperalimentation might have been beneficial.

There has been considerable debate over the merits of pre-operative drainage of the cyst. The potential hazards of drainage are the possibility of intraperitoneal spillage and seeding of ovarian carcinomata, and the increased risks of intra-abdominal infection, haemorrhage and adhesions.[1] The main advantage of drainage is shrinkage of the cyst to a more manageable size, and subsequent ease of operation.[6] Dyspnoea and pulmonary oedema have been described in association with cyst drainage. The mechanism of this is not clear but may be related to the reduction in plasma oncotic pressure that results from a low plasma albumin.[3] Pulmonary oedema may occur when left atrial pressure (mmHg) is equal to 0.57 × plasma albumin (g/litre).[7] This relationship has been studied in patients treated for burns and in patients undergoing major abdominal surgery.[8,9] Transfusion with colloid solutions maintained significantly higher plasma oncotic pressures than transfusion with crystalloids, although pulmonary oedema did not occur in either group. However, it may be relevant that the left atrial pressure remained at low levels (5–10 mmHg) at all times in both groups. According to Bradley,[7] a patient with a plasma albumin concentration of 19 g/litre would be expected to develop pulmonary oedema with a left atrial pressure of 11 mmHg. Our patient (albumin 29 g/litre) would not have been expected to develop pulmonary oedema unless the left atrial pressure exceeded 16 mmHg. In view of this, we considered it safer to maintain our patient's plasma albumin level as near normal as possible by using predominantly colloid solutions for transfusion.

A large volume of intravascular colloid was required to maintain cardiovascular stability pre-operatively. Three litres of HPPF (171 g protein, 102 g albumin) were given over 5 days but there was only a small increase in plasma albumin concentration. We were unable to tell whether plasma proteins leaked into the cyst fluid and contributed to an albumin loss during drainage, although this would have been possible using a labelling technique. The albumin content of the cyst fluid drained pre-operatively was 668.8 g. Hoile[4] suggested that reduction in intra-abdominal pressure during drainage allows dilatation of the splanchnic vascular bed and may cause hypotension. If this is so, the large positive fluid balance noted pre-operatively in our patient may be explained by an increased vascular volume. Hypotension due to aortocaval compression was avoided by nursing the patient on her side. Continuous circulatory monitoring was undoubtedly of value in the avoidance of hypotension during cyst drainage.

Operative management

The patient received two general anaesthetics, the first to allow insertion of drains into the cyst and the second for cyst resection. On both occasions, the patient was too large to be placed on one operating table. Sedative or hypnotic premedication was not prescribed because of anxiety on the part of the team that ventilatory depression might result. In retrospect, this was improbable since the patient's ventilatory function was clinically adequate, although no definitive tests were performed.

The trachea was not intubated for anaesthesia while the drains were inserted, although this may have increased the risk of regurgitation.[10] This policy was adopted for several reasons. The patient was not in labour, had not received an opioid,[11] had been starved for at least 8 hours pre-operatively so that the volume of gastric contents was likely to be approximately 30 ml,[12] and an antacid mixture had been administered. She had not admitted to acid reflux pre-operatively[13] and was to be anaesthetised in the left lateral position for a short period. In addition, it was felt that this technique would reduce the risk of sore throat, suxamethonium pains and chest infection, all of which might jeopardise future surgery in a patient with a bizarre psychological background. The use of a histamine H_2-receptor blocker might have been a useful adjuvant.[14]

Etomidate was chosen for induction because of its stable effect on cardiovascular performance. The choice of enflurane during the first anaesthetic avoided the possibility of multiple exposure to halothane. During anaesthesia for resection of the cyst, pancuronium was selected because of its lack of cardiovascular depression, although it can produce tachycardia. In addition, anaphylactoid reactions are unreported. However, in future we would consider muscle relaxants of shorter duration of action, administered as an infusion, e.g. atracurium.

The gradual decrease in $P\text{a}o_2$ during the procedure may have several physiological causes. Retraction of abdominal contents and restriction of ventilation due to abdominal packs, may have caused a reduction in functional residual capacity. In addition, reduction in cardiac output and pulmonary blood flow during the period of hypotension probably increased venous admixture. This effect would not be improved by the application of PEEP, which would tend to reduce pulmonary blood flow further. It is notable that $P\text{a}o_2$ did not improve until the circulation had returned to normal.

It is important to ensure that intravenous cannulae are adequate to cope with the expected rate of transfusion. Episodes of hypotension occurred during surgery, unassociated with changes in venous pressure, and serve to demonstrate the inadequacy of CVP monitoring as a guide to circulating blood volume and ventricular function.

Our patient lost an estimated 10 litres of blood intra-operatively and it is likely that peripheral vasoconstriction was intense. The left atrial pressure reflects circulating volume more accurately when left ventricular function is normal, since it is free from the effects of venous vasoconstriction. Measurement of pulmonary capillary wedge pressure would have been of value during the operation.

Surgical technique is of obvious importance with regard to dissection and excision of the cyst but it is equally important with regard to wound closure. Redundant abdominal wall between the rectus muscle should be excised and a binder applied in order to reduce abdominal distension.[4] In addition, laxity in the abdominal wall may affect ventilatory function adversely. By allowing the rib cage to expand by elastic recoil, it may adopt a resting position nearer the top of its pressure–volume curve, resulting in inefficient expansion during breathing. It was interesting that tightening the abdominal binder improved ventilatory function postoperatively, possibly by preventing recoil of the rib cage to a larger lung volume.

Postoperative care

In contrast to the problems encountered by others, our patient's postoperative management was relatively uncomplicated. The degree of hypovolaemia may be underestimated.[3,4,6]

Hypovolaemia as judged by hypotension, low CVP and cool vasoconstricted peripheries persisted for 12 hours despite transfusion of large volumes of cystalloid and colloid solutions. Peripheral perfusion was improved during transfusion by the use of vasodilators. Blood coagulation may be abnormal postoperatively. Clotting factors and platelets are consumed during normal coagulation and are inadequately replaced by a large transfusion of bank blood. This problem is largely avoided by anticipation and treatment with fresh frozen plasma and platelets.

Ventilatory distress postoperatively may stem from defects in several systems. Six of eight reported cases encountered ventilatory difficulty.[1–6] Mechanical compression of the thoracic contents by the cyst pre-operatively, by packs and retractors intra-operatively and by abdominal binders postoperatively, may cause a reduction in tidal volume, vital capacity and functional residual capacity. It is also likely that excision of the cyst and repair of the abdominal wall alter the mechanics of diaphragm and chest wall movement. Close liaison with the physiotherapist is of value in overcoming these problems and in prevention of infection.

Postoperative pain may contribute to ventilatory disability and was managed satisfactorily in this case by the use of a phenoperidine infusion, although it may be argued that regional analgesia using epidural local anaesthetics or opioids would have provided better relief.

Pulmonary oedema has been described following cyst drainage and in the postoperative period, and contributes to ventilatory dysfunction.[3,4] This may be associated with low levels of plasma albumin, but pulmonary oedema may occur after large transfusions of crystalloid and colloid, and in left ventricular failure. Since clinically the left ventricular function of our patient was good, and when warm and haemodynamically stable her right atrial pressure was only 5 cm H_2O, we suggest that the mild pulmonary oedema which occurred, was due to pulmonary capillary leakage.

Postoperative hypothermia may largely be avoided by prevention of intra-operative heat loss. The use of a warming blanket and vasodilators enabled our patient to re-attain normothermia within 12 hours.

Intestinal ileus has been reported in several cases. Gaseous distension of the abdomen (meteorism) has also been described and has led to death in one case.[1] The risk of both is thought to be reduced by the use of an abdominal binder.[4] Intravenous feeding was commenced on the first postoperative day, partly in anticipation of ileus but also in view of the patient's poor general nutritional status. However, an ileus did not develop and oral feeding was started on the third postoperative day.

Patients who present with giant ovarian cyst are often elderly and debilitated, and have venous congestion of the legs. They are therefore at risk from deep venous thrombosis and pulmonary embolism. Prophylaxis used in this case included postoperative stockings, intravenous Dextran 70 and rapid mobilisation. Subcutaneous heparin was considered unsuitable because of the risk of massive haemorrhage.

References

1. SYMMONDS RE, SPRAITZ AF, KOELSCHE GA. Large ovarian tumor. Report of a case. *Obstetrics and Gynecology* 1963; **22:** 473–7.
2. HASPELS AA, ZUIDEMA PJ. A giant ovarian cyst in a Javanese woman. *British Medical Journal* 1982; **284:** 1410.
3. DRIFE JO, TROTTER GA. Britain's biggest ovarian cyst? *British Medical Journal* 1981; **283:** 1661–2.
4. HOILE RW. Hazard in the management of large intra-abdominal tumours. *Annals of the Royal College of Surgeons* 1976; **58:** 393–7.
5. HUNTER DJS. Management of a massive ovarian cyst. *Obstetrics and Gynecology* 1980; **56:** 254–5.
6. BEZJIAN AA, O'LEARY JA. A massive (121-lb) ovarian tumour—preoperative siphonage and excision. A case report. *Obstetrics and Gynecology* 1971; **38:** 214–6.
7. BRADLEY RD. *Studies in acute heart failure.* London: Edward Arnold, 1977.
8. ZETTERSTRÖM H, ARTURSON G. Plasma oncotic pressure and plasma protein concentration in patients following thermal injury. *Acta Anaesthesiologica Scandinavica,* 1980; **24:** 288–94.
9. ZETTERSTRÖM H, HEDSTRAND U. Albumin treatment following major surgery. I. Effects on plasma oncotic pressure, renal function and peripheral oedema. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 125–32.
10. TAYLOR G. Acid pulmonary aspiration syndrome after antacids. A case report. *British Journal of Anaesthesia* 1975; **47:** 615–6.
11. HOLDSWORTH JD. Relationship between stomach contents and analgesia in labour. *British Journal of Anaesthesia* 1978; **50:** 1145–8.
12. BLOUW R, SCATLIFF J, CRAIG DB, PALAHNIUK RJ. Gastric volume and pH in post-partum patients. *Anesthesiology* 1976; **45:** 456–7.
13. BROCK-UTNE JG, DOW TGB, DIMOPOULOS GE,

Anaesthesia, 1987, Volume 42, pages 975–979

CASE REPORT

Combined unilateral high frequency jet ventilation and contralateral intermittent positive pressure ventilation

B. A. MORGAN, D. PERKS, I. D. CONACHER AND M. L. PAES

Summary

The anaesthetic management of a patient who required right lower lobectomy for bronchial carcinoma associated with emphysema, pneumoconiosis and a previous thoracoplasty for pulmonary tuberculosis, is described. A technique of unilateral high frequency jet ventilation plus conventional intermittent positive pressure ventilation to the contralateral lung was used.

Key words

Ventilation; high frequency jet, intermittent positive pressure.

During lung surgery the rhythmic lung expansion produced by bilateral intermittent positive pressure ventilation (IPPV) may hinder difficult surgical procedures. Conventional anaesthetic practice for intrathoracic procedures involves controlled ventilation of one lung and the use of muscle relaxants. Patients with pre-existing diffuse lung pathology who require partial lung resection for discrete conditions, present particular difficulty because they may not tolerate the unilateral ventilation associated with the use of a conventional double lumen tube, despite measures to optimise gas exchange such as continuous positive airway pressure (CPAP) to the nonventilated upper lung.[1]

Asynchronous independent lung ventilation (AILV) through a double lumen tube has been used to treat acute unilateral disease[2–4] but does not appear to have been attempted during anaesthesia for partial lung resection. High frequency jet ventilation (HFJV) has been used with success in patients with unilateral and bilateral lung pathology.[5,6]

Case history

A 60-year-old retired miner, weight 58 kg, required right lower lobectomy for histologically proven squamous cell carcinoma. He contracted pulmonary tuberculosis at the age of 24 years which required sanatorium treatment and a left thoracoplasty. Deterioration of his lung function had led to early retirement 6 years previously. He had been a life-long cigarette smoker and was noted to have hypertrophic pulmonary osteoarthropathy (HPOA). He presented with an 18-month history of haemoptysis; bronchoscopy and fine needle aspiration confirmed the suspected carcinoma.

Drug therapy at the time of operation consisted of bronchodilators (salbutamol inhaler as required, salbutamol 4 mg three times a day

---

B.A. Morgan,* FFARCS, D. Perks, FFARCS, Senior Registrars, I.D. Conacher, MRCP, FFARCS, M.L. Paes, FFARCS, Consultants, Department of Cardiothoracic Anaesthesia, Freeman Hospital, Newcastle-upon-Tyne NE7 7DN.

* Present address: Dr B.A. Morgan, Consultant, Department of Anaesthetics, Royal Shrewsbury Hospital, Mytton Oak Road, Shrewsbury.

0003–2409/87/090975 + 05 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

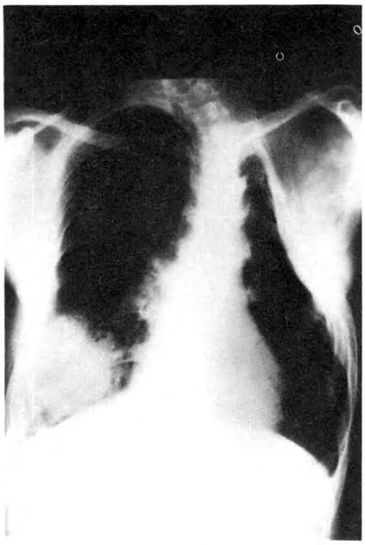


Fig. 1. Pre-operative chest X ray.

orally) and diclofenac 50 mg three times a day for pain relief. Pre-operative chest X ray (Fig. 1) showed the old left thoracoplasty, a hyperinflated right upper lobe with diffuse emphysematous changes, and a solid lesion in the right lower lobe. Spirometry showed FEV_1 1.50 litres, FVC 2.10 litres, with FEV_1/FVC 73% of predicted. A ventilation–perfusion lung scan indicated that 65% of overall function was in the right lung. In spite of this, and in the presence of normal liver and bone scans, he was felt to be a candidate for right lower lobectomy.

The opinion of anaesthetists was that the patient would probably not tolerate conventional one lung anaesthesia but that operation was feasible provided that the dependent lung (thoracoplasty) was not subjected to high ventilatory pressures and that some method could be found to recruit alveoli from the operative lung.

The patient was premedicated with temazepam 10 mg and metoclopramide 10 mg orally one hour pre-operatively. Anaesthesia was induced after 5 minutes of pre-oxygenation, with intravenous fentanyl 100 μg and thiopentone 185 mg, and muscle relaxation produced by vecuronium 6 mg. An adult Negus bronchoscope was passed, whilst ventilation and oxygenation were provided using a Sanders injector. The bronchoscope was removed after assessment of the operability of the tumour by the surgeon, and intubation with a medium left Robertshaw double lumen tube performed. A radial arterial line allowed direct measurement of blood pressure and blood gas tensions. IPPV to both lungs and anaesthesia were then maintained by a Fluidor 2 anaesthetic ventilator driven from a Boyle 2000 machine, using nitrous oxide 65%, oxygen 35% and isoflurane 0.5%.

When the chest was opened through a right thoracotomy, with ventilation of the left lung only, oxygenation was adequate with $F\text{IO}_2$ 0.5 but $P\text{aCO}_2$ had increased (Table 1) and HFJV to the right lung was commenced. This was performed by an Acutronic MK800 clinical ventilator, a high frequency jet ventilator electronically cycled for use with air or oxygen–air mixtures and with an input pressure of 0–5 bar and a frequency rate variable between 2 and 600 cycles/minute, at inspiratory times of 10–70% of total; this provides a minute volume of between 5 and 50 litres/minute. The air–oxygen mixture ($F\text{IO}_2$ 0.5) was delivered through a 16-G metal cannula and connector[7] situated distally on the right limb of the Robertshaw tube. Driving gas pressure was 2 bar, driving gas volume 20 litres/minute, frequency 100 cycles/minute, with inspiration time set at 30%. Conventional ventilation continued to the dependent left lung (Fig. 2).

This arrangement maintained oxygenation and reduced $P\text{aCO}_2$ (Table 1) for the duration of surgery. (Surgical compression of the operative right lung caused an increase in $P\text{aCO}_2$ which was alleviated by increasing the driving gas pressure to 3 bar.) The pulsation of the operative lung HFJV at 100 cycles/minute did not disturb the surgeon and the lung did not deflate or hyperinflate. HFJV was discontinued after 26 minutes, once the right lower lobe was resected. Positive measures to reflate the right lung were not required. The patient's trachea was extubated following reversal of neuromuscular blockade with intravenous neostigmine 2.5 mg and glycopyrronium 0.6 mg, and he recovered consciousness within 5 minutes. He was then returned to the high dependency unit with a bupivacaine infusion via a paravertebral catheter to provide postoperative analgesia. His recovery was uneventful and he was discharged on the eighth postoperative day.

Discussion

High frequency jet ventilation has been in use clinically for 10 years[8–16] and is based on the

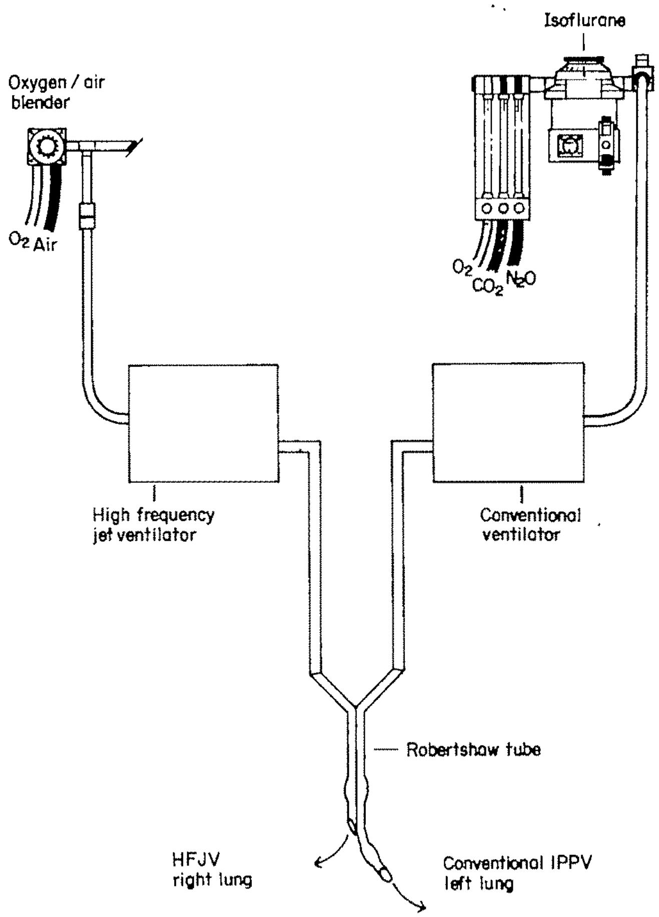


Fig. 2. Diagrammatic illustration of the combined IPPV–HFJV arrangement.

Table 1. Patient data.

Ventilation method	pH	Pa_{O_2} (kPa)	Pa_{CO_2} (kPa)	Base excess (mmol/litre)	F_{IO_2}	IPPV Respiratory rate (breaths/minute)	HFJV Cycles/minute	HFJV $\dot{V}$ (litres/minute)
Conventional IPPV both lungs	7.43	23.2	4.9	+0.1	0.35	12	0	0
Conventional IPPV left lung only	7.38	13.1	6.8	+0.2	0.5	12	0	0
Conventional IPPV left lung, HFJV right lung	7.40	14.5	5.6	+0.2	0.5	12	100	20
As above, but with surgical compression of right lung	7.35	15.0	7.3	+0.3	0.5	12	100	20
As above, but after increasing driving gas pressure to 3 bar	7.40	29.0	5.1	−1.0	0.5	12	100	20
As above	7.41	21.3	5.2	0	0.5	12	100	20
Conventional IPPV both lungs, surgery completed	7.40	15.8	5.6	+0.1	0.35	12	0	0

physical principle of the jet injector, in which a high pressure gas source (60–270 kPa) is used to overcome the resistance of a narrow cannula, to deliver 100–200 msec pulses into the upper airway via a gating mechanism which may be fluidic,[17] pneumatic[14] or solenoid valve.[18] Tidal volume, rates of entrained to directly delivered gases, bias flow, cycle rate and I:E ratio all have different physiological implications during HFJV.

The advantages are claimed to be a reduction in pulmonary barotrauma,[19,20] lower peak airway pressures and improvement in gas exchange, particularly in diseased lungs, by recruitment of alveoli with abnormal time constants. HFJV has been used successfully during lobectomy;[21] however, inhalational anaesthesia was not possible with the system used and intravenous thiopentone and fentanyl were required.

Our patient's severe pulmonary impairment caused by a combination of parenchymal lung disease and previous thoracoplasty, led us to consider ventilation of the upper lung with HFJV in order to provide a relatively immobile surgical site as well as to augment gas exchange. The lower lung was ventilated conventionally (IPPV) and this permitted maintenance of anaesthesia with isoflurane at low inflation pressures. The known problems of high dose opiates or continuous intravenous anaesthetic infusion techniques were thus avoided. We believed that a prolonged period of postoperative respiratory support would have been most undesirable for this patient.

The combined technique provided satisfactory anaesthesia, good operating conditions, adequate gas exchange and permitted rapid postoperative recovery; in addition, it proved to be technically straightforward. The authors would recommend it for consideration in any patient who presents for partial lung resection in the presence of severe pulmonary impairment.

Acknowledgments

Our grateful thanks are due to Miss H. Ashford and Miss A. Wilson for typing the manuscript and to D. Crawford, ODA for the line diagram (Fig. 2).

References

1. Benumof JL. One-lung ventilation and hypoxic pulmonary vasoconstriction: implications for anesthetic management. *Anesthesia and Analgesia* 1985; **64:** 821–33.
2. Stow PJ, Grant I. Asynchronous independent lung ventilation. *Anaesthesia* 1985; **40:** 163–6.
3. Powner DJ, Eross B, Grenvick A. Differential lung ventilation with PEEP in the treatment of unilateral pneumonia. *Critical Care Medicine* 1977; **5:** 170–2.
4. Hillman KM, Barber JD. Asynchronous independent lung ventilation. *Critical Care Medicine* 1980; **8:** 390–5.
5. Nishimura M, Takezawa J, Nishimura MK, Taenaka N, Shimada Y, Yoshiya I, Fujimoto Y. High-frequency jet ventilation for differential lung ventilation. *Critical Care Medicine* 1984; **12:** 840–1.
6. McCarthy G, Coppel DL, Gibbons JR, Gosgrove J. High frequency jet ventilation for bilateral bullectomy. *Anaesthesia* 1987; **42:** 411–4.
7. Conacher ID. A Venturi connector for tracheal tubes. *Anaesthesia* 1985; **40:** 566–8.
8. Heijman K, Heijman L, Jonzon A, Sedin G, Sjöstrand U, Widman B. High frequency positive pressure ventilation during anaesthesia and routine surgery in man. *Acta Anaesthesiologica Scandinavica* 1972; **16:** 176–87.
9. Eriksson I, Nilsson LG, Nordström S, Sjöstrand U. High-frequency positive-pressure ventilation (HFPPV) during transthoracic resection of tracheal stenosis and during peroperative bronchoscopic examination. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 113–9.
10. Sjöstrand U. Experimental and clinical evaluation of high-frequency positive pressure ventilation. *Acta Anaesthesiologica Scandinavica* 1977; **64** (Suppl): 1–178.
11. Babinski M, Klain M, Smith RB. High-frequency jet ventilation. *American Society of Anesthesiologists Annual Meeting, New Orleans, Louisiana, 15–19 October 1977*: 781 (Abstract).
12. Carlon GC, Kahn RC, Howlands WS, Ray C Jr, Turnbull AD. Clinical experience with high frequency jet ventilation. *Critical Care Medicine* 1981; **9:** 1–6.
13. Babinski M, Smith RB, Klain M. High frequency jet ventilation for laryngoscopy. *Critical Care Medicine* 1980; **8:** 243.
14. Sjöstrand U. High-frequency positive-pressure ventilation—a review. *Critical Care Medicine* 1980; **8:** 345–64.
15. Baum M, Benzer H, Geyer A, Mutz N. Gas-exchange and flow properties during high-frequency jet ventilation. *Critical Care Medicine* 1981; **9:** 159.
16. Borg U, Eriksson I, Sjöstrand U, Wattwil M. Experimental studies of continuous positive-pressure ventilation (CPPV) and high-frequency positive-pressure ventilation (HFPPV). *Resuscitation* 1981; **9:** 1–21.
17. Klain M, Smith RB. High frequency percutaneous transtracheal jet ventilation. *Critical Care Medicine* 1977; **5:** 280–7.
18. Carlon GC, Miodownik S, Ray C Jr, Kahn RC. Technical aspects and clinical implications of high

frequency jet ventilation with a solenoid valve. *Critical Care Medicine* 1981; **9:** 47–50.

19. Whitwam JG. Functional dead space during high frequency ventilation. *European Journal of Anaesthesiology* 1984; **1:** 7–9.
20. Gallagher TJ, Klain M, Carlon GC. Present status of high frequency ventilation. *Critical Care Medicine* 1982; **10:** 613–7.
21. Smith RB, Hoff BH, Rosen L, Wilson E, Swartzman S. High frequency ventilation during pulmonary lobectomy—three cases. *Respiratory Care* 1981; **26:** 437.

Anaesthesia, 1987, Volume 42, pages 980–983

CASE REPORT

Ketamine infusion

Its use as a sedative, inotrope and bronchodilator in a critically ill patient

G. R. PARK, A. R. MANARA, L. MENDEL AND P. E. BATEMAN

Summary

A patient with acute lymphatic leukaemia developed a bilateral fulminating Pseudomonas aeruginosa pneumonia and required controlled ventilation of the lungs. Marked agitation, hypotension and bronchospasm unresponsive to conventional bronchodilators presented a therapeutic challenge. A continuous intravenous infusion of midazolam failed to provide adequate sedation. A continuous intravenous infusion of ketamine resulted in better sedation, an increase in arterial pressure and a dimunition of bronchospasm. The clinical improvement was maintained for the 5 days during which ketamine was infused. Plasma concentrations of ketamine and its metabolites are reported.

Key words

Anaesthetics, intravenous; ketamine.
Intensive care; sedation.

Case history

A 24-year-old man, weight 65 kg, with a 2-month history of acute B-cell lymphatic leukaemia treated with cytotoxic drugs, was admitted to the intensive care unit (ICU) with respiratory failure due to a bilateral pneumonia. The organism responsible was identified as *Pseudomonas aeruginosa*. He was known to have asthma and bronchiectasis for which he received salbutamol and betamethasone by inhalation.

Investigations on admission to the intensive care unit included haemoglobin (10.8 g/dl), white cell count (0.3×10^9/litre) and platelets (6×10^9/litre). Arterial blood gas analysis showed a hydrogen ion concentration of 30.3 nmol/litre, $P\text{aCO}_2$ 4.5 kPa, $P\text{aO}_2$ 16.8 kPa ($F\text{IO}_2$ 0.6) and base excess 5.5 mmol/litre. Liver function tests and plasma urea and electrolyte concentrations were normal. His APACHE II score[1] on admission was 26. Initial treatment included antibiotics, supplemental oxygen, nebulised salbutamol and hydrocortisone.

The patient's condition deteriorated; arterial hypoxaemia worsened and periods of hypotension required inotropic support. Mechanical ventilation of the lungs was started on the second day when his $P\text{aO}_2$ was 6.0 kPa ($F\text{IO}_2$ 0.5) and resulted in an immediate improvement in oxygenation; however, marked bronchospasm was

---

G.R. Park, BSc, FFARCS, Consultant, A.R. Manara,* MRCP, FFARCS, Research Registrar, L. Mendel, FFARACS, Research Fellow, The Intensive Care Unit, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, P.E. Bateman,† BSc, Chief Technician, Clinical Research Centre, Division of Anaesthesia, Watford Road, Harrow, Middlesex.

* In receipt of a grant from Napp Laboratories Ltd.

† Present address: MRC Clinical Pharmacology Unit, University Department of Clinical Pharmacology, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE.

Correspondence should be addressed to Dr G.R. Park please.

0003–2409/87/090980 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

present despite administration of nebulised salbutamol 10 mg 2-hourly.

It proved to be difficult to establish a level of sedation which allowed mechanical ventilation without struggling; an infusion of midazolam of up to 10 mg/hour and neuromuscular blockade with pancuronium 2–4 mg 2–4-hourly were necessary to achieve adequate ventilation. On day 3 the bronchospasm became worse, although arterial blood gases were unchanged. He was also hypotensive; this was exacerbated by his sedation and required treatment with 3 μg/kg/minute of dobutamine.

A ketamine infusion was started to resolve the problems of inadequate sedation, hypotension and bronchospasm. Ketamine is known to reduce airway resistance in patients with pulmonary dysfunction,[2] to produce sedation[3] and increase arterial pressure.[4] An intravenous bolus of ketamine (20 mg) was administered initially. The bronchospasm improved on auscultation and there was a decrease in peak inspiratory pressure of 0.4 kPa; the patient appeared to be more comfortable and tolerated mechanical ventilation better. A continuous intravenous infusion of ketamine was started at 20 mg/hour and was increased by increments of 20 mg to 100 mg/hour; at this infusion rate, the patient was roused by pain only. His systolic arterial pressure increased, from 90–120 mmHg before ketamine administration, to 135 mmHg and this was sustained throughout the duration of the infusion. There was also a reduction in heart rate from 120 to 85 beats/minute. The cardiovascular improvement allowed the dobutamine to be stopped.

The next day, the ketamine infusion was decreased to 75 mg/hour and the patient awoke very quickly; 10 mg diamorphine was administered with minimal effect and the ketamine infusion rate was restored to 100 mg/hour.

The infusion rate was reduced to 25 mg/hour on the third day of ketamine administration to assess the patient's mental state. Consciousness returned quickly and the dose of ketamine was increased to 50 mg/hour. Ketamine was stopped after 5 days; midazolam was administered for a further 16 hours before an attempt was made to wean the patient from the ventilator. He required reventilation of his lungs after 3 hours but, during this period, was lucid and did not admit to any hallucinations or unusual dreams. Ketamine was not restarted because of the lack of familiarity and knowledge about possible ill effects of long-term infusion. The patient had received ketamine for 102.5 hours; the total dose infused was 7854 mg at an average rate of 76.6 mg/hour (19.6 μg/kg/minute). There had been only minimal wheeze and cardiovascular stability had been maintained.

Blood samples for measurement of plasma concentrations of ketamine and its metabolites were taken when the patient was thought to be in a steady state and when the rate of infusion was changed. These samples were collected from an indwelling arterial line both during and after the ketamine infusion at the times shown in Fig. 1. The blood was centrifuged at 3000 r.p.m. for 15 minutes and the supernatant plasma separated and stored at −20°C prior to analysis for concentration of ketamine and its major metabolites (norketamine and dehydronorketamine) by high pressure liquid chromatography. The results are shown in Fig. 1.

Subsequent course

Sedation by means of simultaneous infusions of midazolam, thiopentone and diamorphine was required for a further 10 days, during which time the patient continued to maintain clinical improvement with gradual resolution of the pneumonia. He was weaned successfully from mechanical ventilation on day 16.

Despite continuation of the midazolam infusion over the next 4 days, the patient became very frightened and distrusted the nursing staff. The patient returned to the ward after 21 days in the ICU. Over the next week he was emotionally labile with sleep disturbances and forgetfulness, and suffered marked guilt feelings about racist dreams. These symptoms gradually lessened and he was cheerful and no longer troubled by nightmares when he visited the ICU 31 days after discharge.

Discussion

Experience with long-term infusions of ketamine is limited. This report describes the successful use of a ketamine infusion over a 5-day period to provide sedation and to relieve bronchospasm. Ketamine has been reported to relieve bronchospasm at the induction of anaesthesia[5] and in patients who breathe spontaneously[6] or during mechanical ventilation of the lungs.[7]

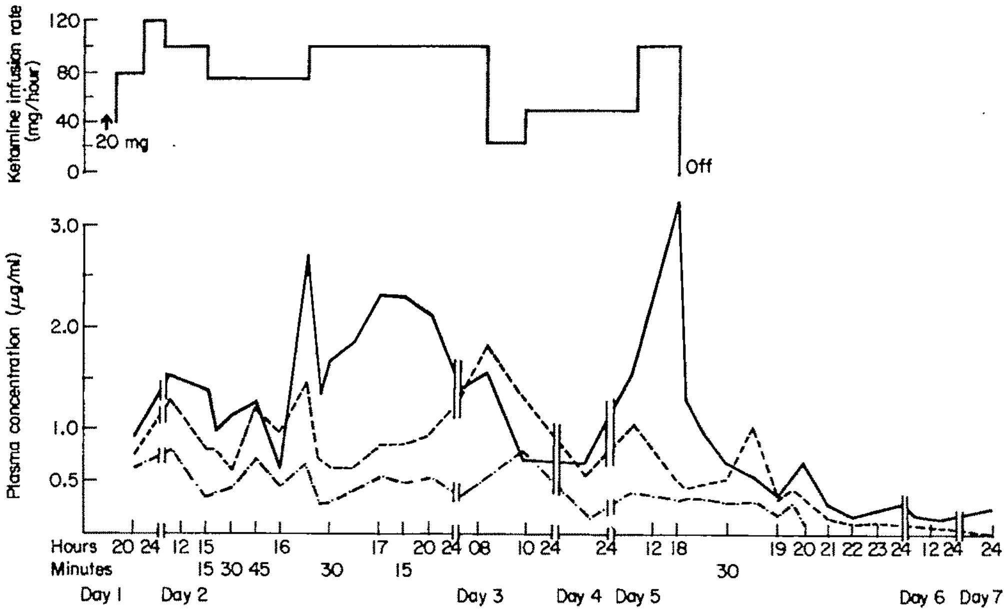


Fig. 1. Plasma concentrations of ketamine and its major metabolites during and after continuous intravenous infusion of ketamine. ——, Ketamine; – – –, dehydronorketamine; –·–·–, norketamine.

Controlled sedation has become more difficult in patients who require intensive care since the withdrawal of Althesin and the demonstration of adrenal suppression with etomidate.[8] Midazolam, whilst a useful agent, does not always provide satisfactory sedation.[9] Adequate sedation for this patient proved to be difficult in spite of an intravenous infusion of midazolam and bolus doses of opiates. The use of ketamine to achieve both sedation and bronchodilation proved successful, and also increased arterial pressure.

Since the plasma concentration of ketamine in this patient was rarely above 2.7 µmol/litre (the level at which patients normally recover consciousness[10]), it appears that ketamine exerts inotropic and bronchodilator effects at subanaesthetic plasma concentrations. It is likely that the patient was adequately sedated at lower plasma concentrations of ketamine because of the concurrent administration of other sedatives.

Concern over psychomimetic effects associated with the use of ketamine, has discouraged its more widespread use for sedation in patients who require intensive care. In this patient there was a lucid period following the withdrawal of ketamine. The concurrent administration of the benzodiazepine midazolam should protect patients from psychomimetic sequelae due to ketamine.[3] When this patient's trachea was extubated following weaning from mechanical ventilation he was again lucid, and was asked specifically about dreams and hallucinations; these were denied. The late psychological problems described are unlikely to be related to ketamine or its metabolites, since none were detected in his plasma at this time. These late disturbances were probably the result of acute withdrawal from opiates, benzodiazepines[11] and barbiturates.

The widespread use of ketamine for sedation in patients who need intensive care cannot be advocated on the basis of experience in a single patient, but its use in low dose should be considered in selected patients with bronchospasm who may or may not require mechanical ventilation and inotropic support.

References

1. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Critical Care Medicine* 1985; **13:** 818–29.
2. Huber FC, Reves JG, Gutierrez J, Corssen G. Ketamine: its effect on airway resistance in man. *Southern Medical Journal* 1972; **65:** 1176–80.

3. Zsigmond EK, Domino EF. Ketamine. Clinical pharmacology, pharmacokinetics and current clinical uses. *Anesthesiology Review* 1980; 7(4): 13–33.
4. Lilburn JK, Dundee JW, Moore J. Ketamine infusions. Observations on technique, dosage and cardiovascular effects. *Anaesthesia* 1978; **33**: 315–21.
5. Rajanna P, Narayana Reddy J, Gupta PK. Ketamine for the relief of bronchospasm during anaesthesia. *Anaesthesia* 1982; **37**: 1215.
6. Strube PJ, Hallam PL. Ketamine by continuous infusion in status asthmaticus. *Anaesthesia* 1986; **41**: 1017–9.
7. Sheref SE. Ketamine and bronchospasm. *Anaesthesia* 1985; **40**: 701–2.
8. Wagner RL, White PF, Kan PB, Rosenthal MH, Feldman D. Inhibition of adrenal steroidogenesis by the anesthetic etomidate. *New England Journal of Medicine* 1984; **310**: 1415–21.
9. Park GR, Shelly MP, Mendel L, Fromant SM. The use of midazolam by infusion for sedation of patients receiving intensive care. In: Bergmann H, Kramar H, Steinbereithner K, eds. *VIIth European Congress of Anaesthesiology 1986, Abstracts* **I**: 320.
10. Idvall J, Ahlgren I, Aronsen KF, Stenberg P. Ketamine infusions: pharmacokinetics and clinical effects. *British Journal of Anaesthesia* 1979; **51**: 1167–73.
11. Power KG, Jerrom DWA, Simpson RJ, Mitchell M. Controlled study of withdrawal symptoms and rebound anxiety after six week course of diazepam for generalised anxiety. *British Medical Journal* 1985; **290**: 1246–8.

Anaesthesia, 1987, Volume 42, pages 984–986

CASE REPORT

Upper limb sympathetic blockade following intercostal nerve blocks

G. PURCELL-JONES, H. M. SPEEDY AND D. M. JUSTINS

Summary

A case of transient sympathetic block of the arm following percutaneous intercostal nerve injections is described and the possible aetiology discussed.

Key words

Anaesthetic techniques, regional; intercostal nerve block.

Concern and debate have arisen about the spread of local anaesthetic solution following intercostal nerve blocks.[1–4] A number of complications have been attributed to unexpected spread of local anaesthetic.[5–11] All such cases described, however, have resulted from intrathoracic nerve block following thoracotomy. We report here an unexpected case of upper limb sympathetic blockade following percutaneous intercostal nerve injections.

Case history

A 36-year-old woman was referred to the pain relief clinic with right-sided abdominal wall pain. Extensive investigations by the referring physicians had excluded any intra-abdominal pathology. Initial intercostal blocks of the right 7th–10th ribs with bupivacaine 0.5% plus adrenaline produced numbness and some relief of her pain. However, pain persisted in the right hypochondrium and lower costal margin. A second set of intercostal injections was therefore carried out at a higher level. Injection of the right 5th–8th intercostal spaces was performed posteriorly, using X ray control to identify the correct level. The injections were carried out using the method described by Moore *et al.*[12] The needle was advanced under the rib 2–3 mm into the intercostal groove, and 4 ml bupivacaine 0.5% with adrenaline was injected into each space following a negative aspiration. The procedure was technically uneventful.

Half an hour after the injections, the patient reported numbness of the lower thorax and upper abdomen with relief of her pain. After a further 90 minutes, whilst still in the recovery ward, she reported that her right arm was red and hot, and had been so since the injections were performed. It was apparent on examination, that she had developed a sympathetic block of the right arm which was markedly vasodilated and hot compared with the other side.

The temperature of the affected right limb, determined by hand-held thermometers, was 36.8°C compared with 28.0°C in the left hand. There was also an obvious difference in sweating between the two sides. The left was damp and clammy, whilst the affected side was dry. This was confirmed with ninhydrin staining of the

---

G. Purcell-Jones, BSc, MRCP, FFARCS, Lecturer, H.M. Speedy, FFARCS, Senior Registrar, D.M. Justins, FFARCS, Consultant, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH.

0003–2409/87/090984 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

finger prints of both hands using the method described by Dhuner *et al.*[13] Routine recovery observations that included blood pressure had been made following the intercostal injections. At no time was hypotension apparent and the patient exhibited no signs of nausea, faintness or indeed any discomfort. The patient later reported that the sensations of warmth and visually apparent vasodilation had persisted for about 8 hours from the time of onset. She did not develop any sensory or motor deficit in the arm, nor a Horner's syndrome.

Discussion

The sympathetic nerve supply to the arm is derived from the sympathetic ganglia adjacent to the 1st–4th thoracic vertebrae. At this level the sympathetic chain lies on the transverse processes of the vertebrae, close to the heads of the ribs and posterior to the pleura, in the paravertebral space. Sympathetic blockade of the upper limb can be achieved by a stellate ganglion block, which allows the spread of solution down to the 4th thoracic ganglion, or by a percutaneous upper thoracic sympathectomy at either the 2nd or 3rd thoracic ganglion.[14] These produce a sympathetic block similar to that which we have described in this patient.

A paravertebral spread of at least two segments, from the 5th intercostal space to the 3rd thoracic ganglion, would have been necessary in this case to explain the clinical observations. Moore[1,2] was unable to demonstrate extrapleural spread following intercostal blocks. However, other workers have shown in live and cadaveric studies,[3,4] that extensive extrapleural and paravertebral spread of injected material can occur if the posterior intercostal membrane is breached. In this case it is probable that the needle pierced the posterior intercostal membrane, which resulted in spread from the 5th intercostal space to the paravertebral space, at least to the level of the 3rd thoracic vertebrae, and thereby caused a prolonged sympathetic blockade of the arm. In view of the extensive anatomical spread noted on performing intercostal blocks[3,4] and the frequency with which this technique is used, it is surprising that sympathetic blockade of the upper thoracic ganglia has not been reported previously, to our knowledge, in the English medical literature.

The only other reported sympathetic effect following intercostal blockade is hypotension and bradycardia, which occurred in anaesthetised thoracotomy patients.[11] This was attributed to sympathetic blockade of thoracic ganglia but could possibly have been the result of either a systemic effect following absorption of local anaesthetic, which is significant following intercostal blocks,[15] or loss of nociceptive induced vasoconstriction and tachycardia. There is no doubt that ipsilateral sympathetic block of the upper limb occurred in this case.

References

1. Moore DC. Intercostal nerve block: spread of India ink injected to the rib's costal groove. *British Journal of Anaesthesia* 1981; **53**: 325–9.
2. Moore DC, Bush WH, Scurlock JE. Intercostal nerve block: a roentgenographic anatomic study of technique and absorption of solution in humans. *Anesthesia and Analgesia* 1980; **59**: 815–25.
3. Nunn JF, Slavin G. Posterior intercostal nerve block for relief of pain after cholecystectomy. Anatomical basis and efficacy. *British Journal of Anaesthesia* 1980; **52**: 253–9.
4. Murphy DC. Continuous intercostal nerve blockade. An anatomical study to elucidate its mode of action. *British Journal of Anaesthesia* 1984; **56**: 627–9.
5. Otto CW, Wall CL. Total spinal anesthesia: a rare complication of intrathoracic intercostal nerve block. *Annals of Thoracic Surgery* 1976; **22**: 289–92.
6. Benumof JL, Semenza J. Total spinal anesthesia following intrathoracic intercostal nerve blocks. *Anesthesiology* 1975; **43**: 124–5.
7. Scholl W, Makowski HV. High spinal anaesthesia following intrathoracic intercostal nerve block. Report of a case. *Anaesthesist* 1977; **26**: 151–2.
8. Sury MRJ, Bingham RM. Accidental spinal anaesthesia following intrathoracic intercostal nerve blockade. A case report. *Anaesthesia* 1986; **41**: 401–3.
9. Gauntlett IS. Total spinal anesthesia following intercostal nerve block. *Anesthesiology* 1986; **65**: 82–4.
10. Gallo JA, Lebowitz PW, Battit GE, Brunner JMR. Complications of intercostal nerve blocks performed under direct vision during thoracotomy: a report of two cases. *Journal of Thoracic and Cardiovascular Surgery* 1983; **86**: 628–30.
11. Skretting P. Hypotension after intercostal nerve block during thoracotomy under general anaesthesia. *British Journal of Anaesthesia* 1981; **53**: 527–9.
12. Moore DC, Bridenbaugh LD. Intercostal nerve block in 4333 patients: indications, technique, and complications. *Anesthesia and Analgesia* 1962; **41**: 1–11.

Anaesthesia, 1987, Volume 42, pages 987–988

CASE REPORT

Persistent pneumothorax treated with continuous positive airway pressure

M. G. ELPHINSTONE AND I. S. GRANT

Summary

A patient who presented with persistent pneumothorax after blunt chest trauma is described. The lung re-expanded partially in response to chest drain suction but some areas remained collapsed. The institution of continuous positive airway pressure on an intermittent basis, was followed by complete re-expansion of the lung and resolution of the pneumothorax.

Key words

Pneumothorax.
Ventilation; continuous positive pressure.

Continuous positive airway pressure (CPAP) applied via a tight-fitting facemask, has been used for the treatment of hypoxic respiratory failure in adults postoperatively,[1] following trauma[2] or in acute cardiogenic pulmonary oedema.[3] We describe a case of persistent pneumothorax that followed blunt chest trauma which was treated successfully by this method.

Case history

An 18-year-old girl was admitted with left-sided rib fractures (6th and 7th) and a large (50%) pneumothorax after she had been trodden on by her horse. She complained of pain on deep inspiration and coughing, but had no dyspnoea at rest and was otherwise well. A 24-FG chest drain was inserted in the 4th intercostal space at the anterior axillary line and a further chest X ray showed near full expansion of the left lung. The drain was clamped at 48 hours but had to be unclamped when the pneumothorax re-accumulated. The lung failed to re-expand despite suction applied to the drain, and a second chest drain was inserted anteriorly in the 2nd intercostal space at the mid-clavicular line, on the sixth day. Drain suction was continued but 10 days after her admission a significant pneumothorax remained and she was referred to the intensive care unit (ICU) for further management.

On admission to the ICU, a chest X ray showed a 25% pneumothorax with marked contusion and collapse of the left lower zone. Suction (0.5 kPa) was continued to the anterior drain, while the non-functioning lateral drain was removed. She was given chest physiotherapy 2-hourly, and CPAP therapy was started using a tight-fitting facemask and the Ambu CPAP system with a positive pressure of 0.8 kPa for 30 minutes in every hour (Fig. 1). The next day the

---

M.G. Elphinstone, MB, BS, FFARCS, Registrar, I.S. Grant, FRCP, FFARCSI, Consultant, Department of Anaesthesia, Ninewells Hospital, Dundee, Scotland DD1 9SY.

0003–2409/87/090987 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

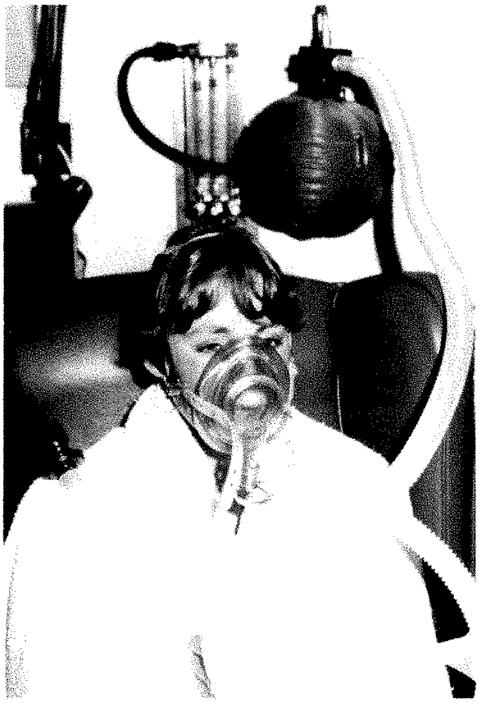


Fig. 1. Ambu CPAP system demonstrated with facemask.

pneumothorax had decreased leaving only a rim, but consolidation and collapse at the left base remained. By the fourth day in the ICU the pneumothorax had resolved completely, chest drain suction was discontinued and the frequency of CPAP therapy reduced to 30 minutes in every 2 hours. The chest drain was removed the following day. Fifteen days after her initial injury the left lung remained fully inflated and she was discharged home with instruction for self physiotherapy.

Discussion

In recent years there has been an increasing trend to treat patients with blunt chest trauma with a conservative regimen that involves CPAP and analgesic therapy, rather than with routine mechanical ventilation. This change in management is based on an understanding of the pathophysiology of the underlying lung injury, which causes interstitial and intra-alveolar haemorrhage and oedema, decreases the functional residual capacity and leads to increased intrapulmonary shunt and hypoxaemia. There is also a concomitant decrease in lung compliance.[4] CPAP has been shown to reverse these changes.[5]

Chest trauma is associated commonly with pneumothorax, which is usually treated readily by pleural drainage. Persistent post-traumatic pneumothorax may result either from a large air leak (bronchopleural fistula) that requires surgical treatment, or from reduced lung compliance and atelectasis, which prevent re-expansion of the lung despite adequate pleural drainage.

Our patient had a persistent pneumothorax of the latter type which would normally require tracheal intubation, mechanical ventilation, intensive physiotherapy and, possibly, bronchoscopy to re-expand the lung. In this instance, the addition of intermittent CPAP by facemask to a regimen of pleural drainage with suction and chest physiotherapy, was followed by rapid re-expansion of a contused and persistently collapsed left lung. Tracheal intubation, mechanical ventilation and bronchoscopy, with their attendant discomfort and morbidity, were avoided. We would suggest that this simple therapy should be considered at an early stage in patients with minor blunt chest trauma who do not require ventilatory support.

References

1. Carlsson C, Sondén B, Thylén U. Can post-operative continuous positive airway pressure (CPAP) prevent pulmonary complications after abdominal surgery? *Intensive Care Medicine* 1981; **7:** 225–9.
2. Linton DM, Potgieter PD. Conservative management of blunt chest trauma. *South African Medical Journal* 1982; **61:** 917–9.
3. Räsänen J, Heikklä J, Downs J, Nikki P, Väisänen I, Vütanen A. Continuous positive airway pressure by face mask in acute cardiogenic pulmonary oedema. *American Journal of Cardiology* 1985; **55:** 296–300.
4. Shackford SR, Virgilio RW, Peters RM. Selective use of ventilator therapy in flail chest injury. *Journal of Thoracic and Cardiovascular Surgery* 1981; **81:** 194–201.
5. Schlobohm RM, Falltrick RT, Quan SF, Katz JA. Lung volumes, mechanics, and oxygenation during spontaneous positive-pressure ventilation: the advantage of CPAP over EPAP. *Anesthesiology* 1981; **55:** 416–22.

Anaesthesia, 1987, Volume 42, pages 989–992

CASE REPORT

Carcinoid syndrome and intravenous cyproheptadine

G. SOLARES, E. BLANCO, S. PULGAR, C. DIAGO AND F. RAMOS

Summary

The anaesthetic management of a patient with the carcinoid syndrome is reported. Important cardiovascular complications occurred immediately after tracheal intubation and during manipulation of metastases. Hypertensive crises were controlled with intravenous cyproheptadine, although hypotension and drowsiness were observed due to its use.

Key words

Pharmacology; cyproheptadine.
Surgery; carcinoid tumour.

The carcinoid syndrome is a constellation of clinical features that occur when certain vasoactive substances are released from a carcinoid tumour. Serotonin, prostaglandins, histamine and kallikreins are some of the amines known to be involved.[1] The carcinoid syndrome is a cause of concern to the anaesthetist, since no specific anaesthetic technique is entirely safe and the pharmacological response to medical treatment is variable.[2] Some reports have been published that did not find special difficulties during management,[3-5] while others have reported serious[6,7] and occasionally fatal complications.[8]

Pre-operative treatment with oral cyproheptadine is often used to diminish the effects of serotonin.[9] However, during anaesthesia other drugs are usually used because cyproheptadine is not generally available in the parenteral form. We describe the anaesthetic management of a carcinoid patient during which important cardiovascular complications occurred and intra-operative hypertensive crises were controlled with intravenous cyproheptadine.

Case history

A 71-year-old male was admitted to the hospital with a clinical diagnosis of carcinoid syndrome. He complained of several attacks per day of facial flushing, colicky abdominal pain, and diarrhoea which had begun 11 months previously. His arterial blood pressure was 130/70 mmHg and a two-dimensional echocardiogram demonstrated no tricuspid or pulmonary valve abnormalities. Twenty-four hour urinary 5-hydroxyindolacetic acid (5-HIAA) levels were 95.5 mg (normal 0–10 mg/24 hours). Computer tomography showed a large mass of 5 × 5 × 9 cm in the right lobe of the liver, suggestive of

---

G. Solares, MD, Staff Anaesthetist, E. Blanco, MD, Resident Anaesthetist, S. Pulgar, MD, C. Diago, MD, F. Ramos, MD, Staff Anaesthetists, Departamento Anestesia y Reanimación, Hospital Nacional Valdecilla, 39008 Santander, Spain.

carcinoid metastases. An exploratory laparotomy was scheduled in order to find the primary tumour.

Anaesthetic management

Pre-operative preparation consisted of oral cyproheptadine 2 mg four times per day and diphenhydramine 50 mg three times per day, both administered 24 hours before the operation. Aprotinin 250 000 IU in saline 250 ml, cimetidine 200 mg in saline 100 ml and hydrocortisone 200 mg were given intravenously one hour prior to anaesthesia.

On arrival at the operating theatre, the patient was premedicated with intravenous fentanyl 50 μg, diazepam 2.5 mg and atropine 0.5 mg. The left radial artery and the right internal jugular vein were cannulated under local anaesthesia. Arterial blood pressure, heart rate, ECG, central venous pressure and urine output were monitored continuously.

Prior to induction of anaesthesia arterial blood pressure was 160/80 mmHg with a pulse rate of 52 beats/minute. Anaesthesia was induced with diazepam 7.5 mg and fentanyl 20 μg, followed by pancuronium 6 mg. Immediately after tracheal intubation the patient developed a red facial flush, arterial blood pressure increased to 200/105 mmHg and heart rate was 62 beats/minute. Cyproheptadine 1 mg intravenously was given twice and arterial blood pressure decreased to 140/80 mmHg. Anaesthesia was maintained with nitrous oxide in oxygen and supplementary doses of fentanyl and pancuronium. The operation continued uneventfully for 30 minutes until the surgeons handled the hepatic metastases. Then a sudden increase of arterial blood pressure to 210/110 mmHg with an increase of heart rate to 104 beats/minute occurred and the face and neck of the patient appeared flushed. A bolus of cyproheptadine 1 mg followed by a continuous infusion of nitroglycerine 30 μg/minute was administered and arterial blood pressure decreased rapidly to 90/50 mmHg. The heart rate increased to 150 beats/minute with a decrease of central venous pressure from 8 to 4 mmHg. The nitroglycerine infusion was discontinued and fluid infused to restore arterial blood pressure to 160/80 mmHg. During resection of the hepatic metastases blood pressure increased to 205/105 mmHg on two further occasions but flushing was present only in one. Both episodes were controlled with intravenous cyproheptadine 2 mg. The patient regained haemodynamic stability after right hepatic lobectomy. No bronchospasm or other features of bradykinin release were noted during the operation.

Surgery consisted of right hepatic lobectomy with individual enucleation of two small metastases in the left hepatic lobe. The primary tumour was localised in the ileum approximately 15 cm from the caecum. It was removed and followed by an end-to-end anastomosis. Histological examination of surgical specimens demonstrated carcinoid tissue.

Postoperative course

The patient was transferred to the intensive care unit, where he remained hypertensive for a period of 6 hours. No flushing or episodes of bronchospasm occurred. The patient regained consciousness 3 hours after the operation but he was lethargic and drowsy for the next 24 hours. Eight months after the procedure the patient had had no further carcinoid attacks.

Discussion

It is commonly accepted[1,2] that the anaesthetic management of carcinoid patients should be based on pre-operative preparation with drugs which block the effects of vasoactive amines, the avoidance of anaesthetics that cause serotonin or histamine release, and close monitoring to facilitate prompt recognition of haemodynamic changes.

Oral cyproheptadine has been reported to afford complete relief of serotoninergic symptoms.[10] In addition, cyproheptadine has been reported to decrease metastatic hepatic tumour size.[11] Aprotinin is a kallikrein–bradykinin inhibitor and has been used successfully to control bradykinin crises.[12] Corticosteroids are lysosomal membrane stabilisers and their administration may be more of prophylactic than therapeutic value.[2] Both H_1 (diphenhydramine) and H_2 (cimetidine) histamine antagonists have been recommended, since histamine release has been implicated in attacks.[13] Pre-operative preparation with a combination of these drugs therefore seems a logical approach.

Several anaesthetic techniques have been proposed for carcinoid patients, although at the moment none has proved superior to the others.[1] In this respect, a diazepam–nitrous oxide–fentanyl sequence is an acceptable choice because of its haemodynamic stability and the short-acting analgesic action of fentanyl.[1]

Significant intra-operative complications have been reported in these patients, particularly during induction of anaesthesia and tumour or metastasis manipulations.[2] Bradykinins are said to be responsible for a blue flush, hypotension and bronchospasm, whereas serotonin is believed to cause a red flush, tachycardia and hypertension.[14] Nevertheless, the role of serotonin as the amine entirely responsible for these effects is certainly debatable.[2,15] Serotonin does not induce flushing when it is injected into carcinoid patients.[16] Furthermore, Törnebrandt *et al.*[17] have demonstrated in anaesthetised patients, that plasma serotonin levels did not correlate with cardiovascular changes during flushing episodes. Additionally, these authors found that patients treated with levopromidazine (a non-specific serotonin antagonist) had greater haemodynamic changes than patients left untreated.[17] On the other hand, Roberts *et al.*[18] found that circulating levels of histamine were closely related to blood pressure changes and flushing in a patient with a gastric carcinoid tumour. However, when somatostatin was used to inhibit the histamine release significant hypertension and bradycardia appeared.[18] These reports thus suggest that blockade of only one vasoactive substance may result in unexpected and contradictory effects.

Cyproheptadine has both antihistamine and antiserotonin actions.[9] Cyproheptadine has been recommended as a continuous infusion when used intravenously.[16] Nevertheless we prefer to use it in small incremental doses, because hypotension and drowsiness are its major side effects.[16] Several hypertensive episodes that occurred during anaesthesia were controlled with bolus doses of intravenous cyproheptadine. However, sudden relative hypotension was observed when nitroglycerine was administered concomitantly. This could be the result of a potentiation of these drugs, since this effect was not seen when both agents were given separately. The patient became and remained hypertensive in the immediate postoperative period. The release of further vasoactive aminines from unrecognised metastates could explain this, since the patient persisted with higher 5-HIAA urinary levels several months after surgery. Delay in recovery and drowsiness are both known to occur in patients with serotonin-secreting carcinoid tumours.[12,19] Nevertheless, in our case both appeared more prolonged than expected. Two contributory factors may account for this: the serotoninergic episode nearly at the end of operation, and the intra-operative administration of cyproheptadine.

In summary, the present report describes the successful use of intravenous cyproheptadine to control a hypertensive oral flushing attack during surgery for carcinoid metastases. However, hypotension may occur if other vasodilators are also administered and the agent may cause postoperative drowsiness.

Acknowledgments

The authors would like to thank R. Fernandez from the Department of Pharmacy, for the intravenous preparation of cyproheptadine, and Dr E. Vidal for permission to study this patient under his care.

References

1. McCammon RL. The gastrointestinal system. In: Stoelting RK, Diertdot SF, eds. *Anesthesia and co-existing disease*. New York: Churchill Livingstone, 1982: 363–77.
2. Mason RA, Steane PA. Carcinoid syndrome: its relevance to the anaesthetist. *Anaesthesia* 1976; **31:** 228–42.
3. Miller R, Patel AU, Warner RRP, Parnez IH. Anaesthesia for the carcinoid syndrome: a report of nine cases. *Canadian Anaesthetists' Society Journal* 1978; **25:** 240–4.
4. Fletcher IR, Carson J. Anaesthesia for carcinoid syndrome. *Anaesthesia* 1983; **38:** 510.
5. Horno Gonzalez R, Gomez-Arnaiz J, Gilsanz F, Avello Garcia F. Síndrome carcinoide y anesteriología. Revisión y aportación personal. *Revista Espanola de Anesteslologia y Reanimacion* 1982; **24:** 348–52.
6. Stone HH, Donnelly CC. The anesthetic significance of serotonin secreting carcinoid tumors. *Anesthesiology* 1960; **21:** 203–12.
7. Jones RM, Knight D. Severe hypertension and flushing in a patient with a nonmetastatic carcinoid tumor. *Anaesthesia* 1982; **37:** 57–9.
8. Biörck G, Axén O, Thorsen A. Unusual cyanosis in a boy with congenital pulmonary stenosis and tricuspid insufficiency. Fatal outcome after angiocardiography. *American Heart Journal* 1952; **44:** 143–8.
9. Mason RA, Steane PA. Anaesthesia for a patient with carcinoid syndrome. *Anaesthesia* 1976; **31:** 243–6.

10. VROOM FQ, BROWN RE, DEMPSEY H, HILL SR JR. Studies on several possible antiserotonin compounds in a patient with the functioning carcinoid syndrome. *Annals of Internal Medicine* 1962; **56:** 941–9.
11. HARRIS AL, SMITH IE. Regression of carcinoid tumor with cyproheptadine. *British Medical Journal* 1982; **285:** 475.
12. DÉRY T. Theoretical and clinical considerations in anaesthesia for secreting carcinoid tumors. *Canadian Anaesthetists' Society Journal* 1971; **18:** 245–63.
13. ROBERTS LJ, MARNEY SR, OATES JA. Blockade of the flush associated with metastatic gastric carcinoid by combined histamine H_1 and H_2 receptor antagonists. *New England Journal of Medicine* 1979; **300:** 236–8.
14. LEAHY J, MOLONEY MA. The carcinoid syndrome. *Irish Journal of Medical Science* 1967; **6:** 269–76.
15. GILLIN JS, WINAWER SJ. Malignant carcinoid syndrome. Manifestations and management. *Drug Therapy* 1983; **13:** 149–58.
16. ROBERTSON JIS, PEART WS, ANDREWS TM. The mechanism of facial flushes in the carcinoid syndrome. *Quarterly Journal of Medicine* 1962; **31:** 103–23.
17. TÖRNEBRANDT K, NOBIN A, ERICSSON M, THOMSON D. Circulation, respiration and serotonin levels in carcinoid patients during neurolept anaesthesia. *Anaesthesia* 1983; **38:** 957–67.
18. ROBERTS LJ, BLOOMGARDEN Z, MARNEY SR, RABIN D, OATES JA. Histamine release from a gastric carcinoid: provocation by pentagastrin and inhibition by somatostatin. *Gastroenterology* 1983; **84:** 272–5.
19. RAWLINSON WAL, MARSH RHK, GOAT VA. Anaesthesia for removal of carcinoid metastasis. *Anaesthesia* 1980; **35:** 585–8.

Anaesthesia, 1987, Volume 42, pages 993–995

CASE REPORT

Recurarisation after vecuronium in a patient with renal failure

M. W. CODY AND F. M. DORMON

Summary

Recurarisation after anaesthesia using the muscle relaxant vecuronium is described. The problems of neuromuscular blockade in renal failure are discussed.

Key words

Complications; recurarisation.
Kidney; failure.

Vecuronium is a competitive neuromuscular blocking drug. It is excreted mainly via the biliary system and has been reported to be safe to use in patients with renal failure.[1] We report a patient with renal failure who developed the features of recurarisation following anaesthesia in which vecuronium was used.

Case history

A 29-year-old woman who weighed 60 kg was scheduled for insertion of a peritoneal dialysis catheter under general anaesthesia. She was an insulin-dependent diabetic of 20 years' standing and this was complicated by chronic renal failure, hypertension, retinopathy and by an infected ulcer and osteomyelitis of the left leg. Her drug therapy included nifedipine, ranitidine and a combination of short- and intermediate-acting insulin. Pre-operative investigations showed haemoglobin 10.9 g/dl, sodium 128 mmol/litre, potassium 4.6 mmol/litre, urea 13 mmol/litre and creatinine 503 mmol/litre. Pre-operative bicarbonate was 7 mmol/litre. Before surgery, blood sugar was controlled using a dextrose and insulin infusion. Premedication consisted of papaveretum 15 mg and hyoscine 0.3 mg one hour pre-operatively.

Anaesthesia was induced with thiopentone 250 mg and fentanyl 100 μg followed by vecuronium 7 mg. The trachea was intubated and the lungs ventilated with a mixture of 70% nitrous oxide in oxygen and enflurane 1%. Ventilation was to normocapnia as assessed by an end tidal carbon dioxide analyser, using a Manley ventilator. Neuromuscular blockade was assessed by the response to a supramaximal train-of-four stimulation of the ulnar nerve at the wrist. A further 3 mg of vecuronium was given 30 minutes after the initial dose, when the surgeon complained of inadequate relaxation. At this time two twitches of the train-of-four were visible.

At the end of the procedure, which took one hour, the train-of-four showed two twitches and reversal of residual neuromuscular blockade was achieved using neostigmine 2.5 mg and atropine 1.2 mg. Spontaneous ventilation was re-established, at which point the train-of-four

M.W. Cody, MB, FFARCSI, F.M. Dormon, MB, FFARCS, Senior Registrars, Department of Anaesthetics, Hammersmith Hospital, Du Cane Road, London W12 0HS.

0003–2409/87/090993 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

showed four twitches of apparently equal magnitude. The patient responded to commands and the trachea was therefore extubated and the nerve stimulator removed.

On arrival in the recovery room she was noted to be less responsive and breathing inadequately. It was assumed that this was a result of central depression due to opioid administration, and doxapram 1 mg/kg was given to stimulate respiration. The nerve stimulator was re-applied and revealed four twitches present in the train. There was no improvement in response to doxapram over the following 5 minutes, and naloxone 0.4 mg was given. Only two twitches of the train-of-four were present on restimulation of the ulnar nerve at this stage. Her lungs were ventilated using a facemask. Arterial blood gas analysis showed pH 7.1, $P\text{a}O_2$ 20.6 kPa, $P\text{a}CO_2$ 6.8 kPa and a base deficit of 14 mmol/litre. The sodium and potassium levels were normal. The train-of-four now showed only one twitch. A diagnosis was made of re-recurarisation due to severe acidosis. Her trachea was intubated with ease and 50 ml sodium bicarbonate 8.4% was given. Repeat blood gas analysis after 5 minutes showed pH 7.24, $P\text{a}O_2$ 24.4 kPa, $P\text{a}CO_2$ 6.0 kPa and a base deficit of 11 mmol/litre. Spontaneous ventilation commenced 10 minutes after administration of the bicarbonate and train-of-four stimulation now showed four twitches with the fourth approximately 20% of the first. Further improvement occurred over the next 5 minutes and she was able to respond to commands but unable to lift her head from her pillow.

It was felt appropriate to administer another dose of neostigmine 2.5 mg and atropine 1.2 mg. This produced marked improvement in the patient's condition, with four twitches of equal magnitude in response to a train-of-four, and she was now able to lift her head off the pillow. Her trachea was therefore extubated. Further monitoring in the intensive care unit revealed chronic acidosis with pH 7.29 and base deficit 8 mmol/litre which improved only with vigorous peritoneal dialysis.

Discussion

Demonstration of a normal response to a train-of-four stimulation prior to extubation followed by loss of this response some minutes later, together with clinical deterioration, suggests the diagnosis of recurarisation in this patient. This diagnosis is supported by the finding of co-existent acidosis.

The contribution of acid–base balance and electrolyte disturbance to the reversal of neuromuscular blockade has been well described.[2] Morbidity and mortality have also been shown to increase markedly if respiratory failure occurs due to residual neuromuscular blockade.[3] Many of the problems associated with the use of muscle relaxants in renal failure appear to have been solved with the introduction of newer generation muscle relaxants, namely atracurium and vecuronium.

Atracurium is non-cumulative, easily reversed and removed by Hofmann elimination and would therefore appear to be the ideal agent to use in renal failure. However, it has been pointed out that its principal metabolite, laudanosine, is epileptogenic,[4] although toxic levels of laudanosine have yet to be demonstrated, even following large doses. Its primary elimination by the Hofmann reaction has also been called into question with the discovery of substantial organ-based elimination.[5]

Vecuronium has also been described recently as a useful relaxant in renal failure.[1] It is easily reversed, appears not to accumulate using clinical doses, and elimination is mainly via the hepatic and biliary route. There is also spontaneous de-acetylation to hydroxy metabolites which have minimal neuromuscular blocking effects.[6] It has been shown that the distribution half-life, the elimination half-life, the steady-state volume of distribution and clearance of vecuronium do not differ significantly between patients with normal renal function and those with renal failure.[7] However, in view of a previous report of recurarisation using a combination of aminoglycoside antibiotics and vecuronium,[8] together with our report of recurarisation due to acidosis, doubts may be raised about the suitability of vecuronium in renal failure.

In this case, the contribution made by the institution of peritoneal dialysis is important. Following the insertion of peritoneal dialysis catheters, the surgeons prefer to institute dialysis before waking the patient up, to ensure the catheter is draining normally. Therefore, 1–2 litres of dialysate are instilled into the peritoneal cavity immediately before reversal. This may reduce ventilation by splinting the diaphragm, and further electrolyte changes may occur in a patient who is already unstable.

In conclusion, we consider that vecuronium may be a safe agent to use when neuromuscular blockade is required for patients with renal failure. In view of recent findings, however, it is not the complete answer and it appears that in the management of neuromuscular blockade in patients with renal failure, there is no substitute for careful attention to acid–base balance and electrolytes both pre- and intra-operatively. A neuromuscular blockade monitor should be an integral part of anaesthesia for patients with renal failure.

References

1. Bevan D, Donati F, Gyasi F, Williams A. Vecuronium in renal failure. *Canadian Anaesthetists' Society Journal* 1984; **31:** 491–6.
2. Feldman SA. Effect of changes in electrolytes, hydration and pH upon the reactions to muscle relaxation. *British Journal of Anaesthesia* 1963; **35:** 546–51.
3. Miller RD, Cullen DJ. Renal failure and postoperative respiratory failure: recurarization? *British Journal of Anaesthesia* 1976; **48:** 253–6.
4. Lanier WL, Milde JH, Michenfelder JD. The cerebral effects of pancuronium and atracurium in halothane-anesthetized dogs. *Anesthesiology* 1985; **63:** 589–97.
5. Fisher DM, Claver Canfell P, Fahey MR, Rosen JI, Rupp SM, Sheiner LB, Miller RD. Elimination of atracurium in humans: contribution of Hofmann elimination and ester hydrolysis versus organ-based elimination. *Anesthesiology* 1986; **65:** 6–12.
6. Marshall IG, Gibb AJ, Durant NN. Neuromuscular and vagal blocking actions of pancuronium bromide, its metabolites, and vecuronium bromide (Org NC45) and its potential metabolites in the anaesthetized cat. *British Journal of Anaesthesia* 1983; **55:** 703–14.
7. Fahey MR, Morris RB, Miller RD, Nguyen TL, Upton RA. Pharmacokinetics of Org NC45 (Norcuron) in patients with and without renal failure. *British Journal of Anaesthesia* 1981; **53:** 1049–52.
8. Kronenfeld MA, Thomas SJ, Turndorf H. Recurrence of neuromuscular blockade after reversal of vecuronium in a patient receiving polymyxin/amikacin sternal irrigation. *Anesthesiology* 1986; **65:** 93–4.

Anaesthesia, 1987, Volume 42, pages 996–997

HISTORICAL NOTE

Brünings' bronchoscopic mask

H. A. CONDON

Summary

A tubular gauze mask suitable for inhalational anaesthesia for bronchoscopy, designed by Wilhelm Brünings, is described.

Key words

Equipment; bronchoscopes.
History; Brünings, Wilhelm.

The literature contains many accounts of ingenious pieces of apparatus designed to overcome special problems in anaesthesia. Brünings' bronchoscopic mask comes into this category and should not be lost to posterity.

Wilhelm Brünings[1,2] (Fig. 1) was born on 31 January 1876. In 1901 he passed the State medical examination in Tubingen. After he had travelled the world as a ship's doctor, he worked in Zurich with Gustav Killian, the 'father of bronchoscopy'. When Killian moved to Friberg he took Brünings with him as his assistant. This association with a pioneer endoscopist led to Brünings' life-long interest in this field. Later he moved to Jena and finally, in 1930, to Munich where in due course he became Professor.

His book on endoscopy was expanded when translated into English and published in 1912.[3] Brünings was a man of wide interests, namely art, literature, music and the theatre, who also designed and made furniture. He died on 3 October 1958. As he wished, nobody attended

Fig. 1. Wilhelm Brünings.

H.A. Condon, FFARCS, The Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London WC1X 8DA.

0003-2409/87/090996 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

his funeral. German otorhinolaryngologists have a prize in his memory.

General anaesthesia for bronchoscopy has always presented problems. Killian used a Trendelenberg anaesthetic funnel attached by a tube to the bronchoscope. Vision was therefore intermittent. Brünings overcome this by designing a tubular gauze mask which was attached to the proximal end of the bronchoscope and on which chloroform was sprinkled (Fig. 2). This provided a large evaporating surface without obstruction of breathing while an unobstructe field of vision was allowed. No doubt, in th continental fashion of the time, the anaestheti was administered by a surgical assistant unde the direction of the surgeon.

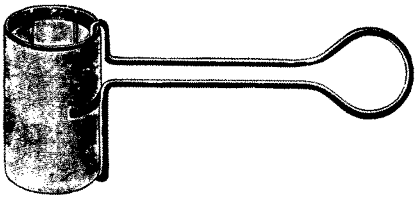


Fig. 2. Tubular bronchoscopic mask.

Acknowledgments

The diagram is reproduced by permission o Messrs Baillière Tindall and I am indebted t Mr P. Zwarts, Library Assistant at the Institut of Laryngology, for translations.

References

1. Leicher H. Wilhelm Brünings zum Gedachtnis *Zeitschrift für Laryngologie, Rhinologie, Otologi und ihre Grenzgebiete* 1959; **38:** 68–71.
2. Kressner A. In memoriam; Professor Dr Med. e Phil. Wilhelm Brünings. *HNO Wegweiser für di Fachaerztliche Praxis* 1959; **7:** 255–6.
3. Brünings W. *Direct laryngoscopy, bronchoscop and oesophagoscopy* (translated by W. Howarth) London: Baillière Tindall and Cox, 1912.

Anaesthesia, 1987, Volume 42, pages 998–1004

SPECIAL ARTICLE

The new generation gelatins

A review of their history, manufacture and properties

J. M. SADDLER AND P. J. HORSEY

Summary

Gelatin solutions of various kinds have been used as intravenous infusions since the First World War and belong to a heterogeneous group of fluids which tend to maintain the colloid osmotic pressure. They are produced by the breakdown of bovine collagen to yield solutions with a range of molecular weights. Anaphylactoid reactions are a rare but well-recognised complication of their use. The solutions help to fill a hiatus that exists between crystalloids and blood products.

Key words

Complications; anaphylactoid reactions.
Intravenous infusion; gelatin solutions.

History

Once the acceptability of intravenous fluid infusions had been established around the turn of the century, clinicians had to decide which solutions were the most beneficial and the debate on this issue continues today.[1] Crystalloid preparations were readily available and inexpensive but they remained within the intravascular compartment only transiently before they were excreted or lost to the interstitial fluid spaces. Following Starling's concept that plasma volume is regulated by the oncotic pressure,[2] attempts were made to find a suitable colloid solution. Human plasma was suitable, but was scarce and expensive. Of the artificial preparations, the vegetable colloids such as acacia, pectin and gum arabic enjoyed a vogue[3,4] and were used for a time in the management of hypoproteinaemic states, e.g. the nephrotic syndrome.[5] They gradually fell into disuse when a variety of unwanted side effects came to light; these included agglutination and interference with hepatic function.[6,7]

Gelatin, a macromolecular protein found in mammals, had potential as a colloidal solution. It was inexpensive, readily available, could be stored over long periods without degradation and seemed to possess low antigenic properties. It was thought that enzymatic pathways in man could split the compound to yield molecules which could be excreted or metabolised. However, gelatin also possessed the disadvantages of a high viscosity in solution, due to the molecular weight of 100 000, and preparations tended to gelate at lower temperatures.

The first reports of the use in man of gelatin solutions appeared in 1915, when transfusion of blood was both difficult and potentially dangerous. It was realised then that salt solutions of

---

J.M. Saddler, MB, ChB, FFARCS, Registrar, P.J. Horsey, MB, BS, FFARCS, Consultant, Shackleton Department of Anaesthetics, Southampton General Hospital, Tremona Road, Southampton SO9 4XY.

0003–2409/87/090998 + 07 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

various kinds produced excellent immediate results in hypovolaemia, but the effect wore off rapidly. Hogan[8] recommended a gelatin solution, which he found efficacious in the resuscitation of moribund hypovolaemic patients. He suggested, perhaps a little prematurely, that 'properly prepared gelatin solutions may be used intravenously without danger'.

Little documented work was performed for several decades after this promising report and it was only during the next World War that there was a rekindling of interest in the potential of gelatin in hypovolaemic states. A clinical trial in 1944 demonstrated that a 5% solution prepared by the Upjohn Company, was useful in resuscitating 50 patients.[9] The increase in plasma volume as measured by the blue azo dye technique, compared favourably with pectin solutions and was greater than that for crystalloids. Eighty percent of the infused gelatin was recovered in the urine.

In 1949, Greaves[10] stated 'reviewing blood substitutes as a whole, the most promising would seem to be a properly prepared gelatin, but it is emphasised that a suitable gelatin is difficult to prepare and must be produced under conditions of rigid control'. It became possible soon after to modify the gelatin macromolecule chemically and so produce a colloid with a smaller average molecular weight.[11] These 'new generation' gelatin plasma substitutes were free from the viscosity and sludging problems of the parent compound and became the progenitors of today's commercial preparations.

Advances in other artificial colloid substances were also made about this time. In Germany, a synthetic compound called polyvinylpyrrolidine (PVP)[12] was produced and used extensively by the German army but later fell into disuse because of long-term storage in the reticuloendothelial system, and possible carcinogenicity. Dextran, a polysaccharide derived from strains of the bacterium *Leuconostoc*, was developed in Sweden[13] and preparations of this substance find clinical applications today.

Enthusiastic reports on gelatin are a feature of earlier American literature[14,15] but the preparations are no longer available in the USA. This is mainly because the earlier products tended to gel on cooling at temperatures higher than would now be acceptable, and thus failed to meet the US Armed Forces requirements that plasma substitutes should remain fluid down to 0°C.

Preparation

Gelatin is prepared by the hydrolysis of collagen (French *collagène*, from Greek *kolla* glue + *-gène* = -GEN producing), the gluey protein found in vertebrates which forms the principal substance in connecting fibres and tissues and in the bones. The collagen molecule consists of three chains of peptides, each of which has a molecular weight of 100 000–120 000, arranged in a three-stranded helical structure. This insoluble compound is converted into gelatin in two stages:[16] first, by the action of alkali, which causes the collagen to swell considerably and ester and peptide links to be hydrolysed; and, second, by the addition of boiling water to form an aqueous solution. The average molecular weight of the gelatin molecules is below 100 000, which suggests that the helices are not simply unravelled during the hydrolysis but that some of the peptide chains, made up of five to seven sub-units, are also split in the process.

If cooled, the preparation forms a reversible gel at a temperature dependent upon the concentration of the solution. This temperature is termed the 'gel melting point'. A 5% solution may have a gel melting point as high as 32°C and this major disadvantage of gelatin led to its disuse as an intravenous colloid. The solution gels at a lower temperature if the collagen is strongly hydrolysed to form gelatin of a low mean molecular weight. However, molecular weights below 18 000 must be obtained to produce a preparation which does not gel in a 5% solution at 0°C. The half-life of such a solution within the circulation would be too short to be of clinical value.

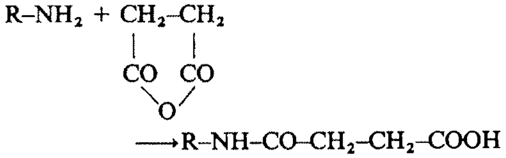
Therefore, in the post-war years, attempts were made to modify the gelatin molecule so that it retains a higher molecular weight, in order to exert a viable osmotic effect, but at the same time possesses a low gel melting point. At present in the United Kingdom there are two types of commercially prepared gelatin solutions for intravenous infusion. They are succinylated gelatin, or modified fluid gelatin, developed in 1952 by Tourtelotte[17] (Gelofusine), and urea-linked gelatin solutions or polygeline, developed in 1962 by Schmidt-Thome *et al.*[18] (Haemaccel). Other types of gelatin solution are available on the Continent, for example Physiogel, Plasmagel and Plasmion, which are similar to Gelofusine, and Gelifundol[11] (oxypolygelatin), the original new generation gelatin.

The urea-linked solution is prepared by cross-linking polypeptides derived from gelatin, each with a molecular weight of 12 000–15 000. Cross-linking utilises a technique often applied in polymer chemistry, using hexamethyl di-isocyanate.[19] The most important reaction is the condensation of a free carboxyl with a free amino group to produce a peptide bond:

$$R_1\text{–}COOH + NH_2\text{–}R_2 \longrightarrow R_1\text{–}CO\text{–}NH\text{–}R_2 + H_2O$$

Other combinations may occur. The product so formed possesses a molecular weight with a number average (*vide infra*) of 24 500, although the molecular weights of the constituent molecules range widely between 5000 and 50 000. The branched peptide chains considerably reduce the gel melting point but still confer a useful colloid osmotic effect through the higher molecular weight. The process is shown in schematic form in Fig. 1.

There are few details on the actual chemical manufacture of succinylated gelatin. The process differs from that of the urea-linked product in that the building blocks of polypeptides have a higher molecular weight of around 20 000, and are modified by the addition of succinic acid anhydride. The following reaction occurs:



$$\longrightarrow R\text{–}NH\text{–}CO\text{–}CH_2\text{–}CH_2\text{–}COOH$$

No cross-linking occurs and the molecular weight is unaltered. Because a basic (NH_2^-) group is removed and replaced by an acidic (–COOH) group, a lower iso-electric point is achieved, with a corresponding increase in the net negative charge. It has been suggested that this increase should augment the osmotic activity at physiological pH, on account of the Donnan effect.[20] This may contribute in part, but it is more likely that the charge changes the chain conformation to produce coils of gelatin which are open. This reduces the diffusion capacity of the molecules, and the retention time within the circulation is significantly prolonged. Disadvantages of this type of modification to gelatin are that the expansion of the molecules increases the viscosity of the solution, and that the gel melting point is not lowered because the molecular weight is unchanged. Figure 2 illustrates the important steps in the production of this product.

Properties

There is no widely accepted generic name for the more recently introduced gelatin preparations. 'Gelatin' itself is unsatisfactory because it describes the macromolecular parent compound. 'Modified gelatin' is often used but is really too close to 'modified fluid gelatin', which has become synonymous with succinylated gelatin. For the purpose of this review the generic term *new generation gelatins* is used for all the chemically modified solutions derived from gelatin.

Molecules of the new generation gelatins vary considerably in size and shape, since the chemi-

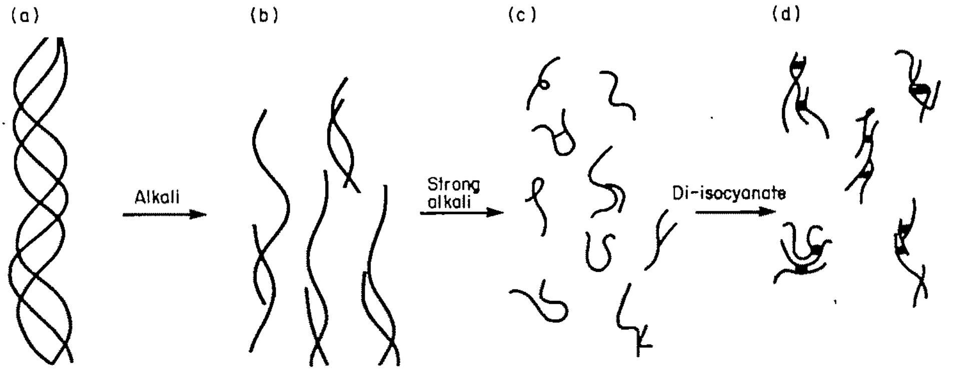


Fig. 1. Schematic representation of the production of urea-linked gelatin from collagen. (a) Collagen (Mw 300 000); (b) gelatin (Mw < 100 000); (c) highly degraded gelatin (Mw 12 000–15 000); (d) urea-linked gelatin (Mw 25 000). ■, Urea linkage.

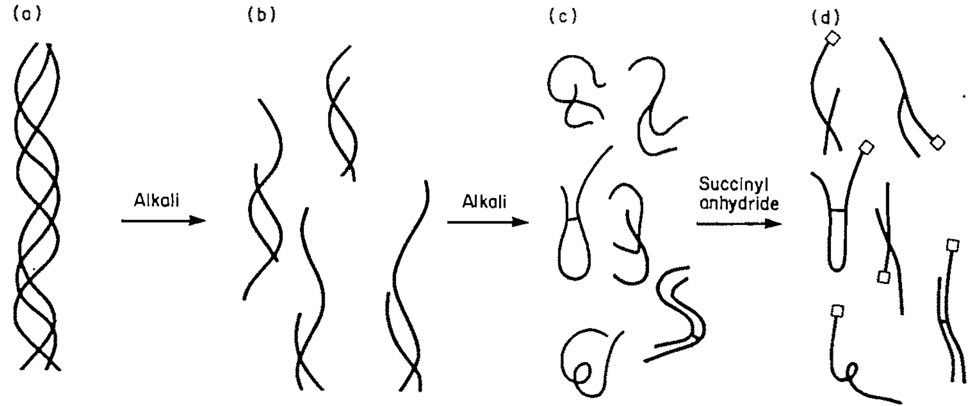


Fig. 2. Schematic representation of the production of succinylated gelatin from collagen. (a) Collagen (Mw 300 000); (b) gelatin (Mw < 100 000); (c) degraded gelatin (Mw 23 000); (d) succinylated gelatin (Mw 23 000). ☐, Succinyl linkage.

cal degradation of gelatin does not yield uniformly sized particles. They can therefore be characterised by an average molecular weight, with smaller and larger molecules dispersed along a normal distribution curve. The average molecular weight of such 'polydisperse colloids' may be classified according to the weight average (Mw) or the number average (Mn). Weight average will always be greater than number average, since the larger molecules contribute more to the measured effect than the smaller ones. Number average values may be more useful since they are more directly related to the oncotic activity. This is an important concept, as manufacturers usually quote the weight average.

'Monodisperse colloids' such as albumin solutions, contain molecules of equal size where Mw and Mn are the same. The advantage of such solutions is that all the molecules are relatively large and remain within the circulation, so that the osmotic pressure effect is sustained. Polydispersity, however, may also confer some advantages. For example, the smaller molecules may initially reduce blood viscosity and promote diuresis, whilst the larger molecules may prolong plasma expansion. Physiochemical properties of various colloids are outlined in Table 1.

It was originally claimed that the new generation gelatins were non-antigenic but all types of product have now been associated with allergic reactions of varying severity. A fatality which incriminated a gelatin product has been reported.[21] Hypersensitivity reactions are, however, also well documented with other types of plasma expanders.

Ring and Messmer's multicentre report[22] on anaphylactoid reactions to colloid volume

Table 1. Physiochemical properties of various colloids.

Colloid	Mw*	Mn	Mw/ Mn	Per cent colloid	Na+ (mmol/ litre)	Cl− (mmol/ litre)	K+ (mmol/ litre)	Ca2+ (mmol/ litre)	Citrate (mmol/ litre)
Succinylated gelatin	35 000	22 600	1.5	4.0	154	125	0.4	0.4	—
Urea-linked gelatin	35 000	24 500	1.4	3.5	145	145	5.1	6.26	—
Dextran 70 in 0.9% saline	70 000	39 000	1.9	6.0	154	154	—	—	—
Human albumin solution	69 000	69 000	1.0	4.5	varies	varies	<2	—	4–10
Hydroxyethyl starch 450/0.7	450 000	70 000	6.4	6.0	154	154	—	—	—

* Mw, Molecular weight (weight average); Mn, molecular weight (number average).

Table 2. Incidence of allergic reactions to plasma expanders (after Ring and Messmer[22]).

Colloid	Number of infusions registered	Total number of reactions	Number of severe reactions (grades 3 or 4)	Total incidence (%)
Human albumin	60 048	7	2	0.011
Dextran 40	51 261	4	1	0.007
Dextran 60/75	34 621	24	6	0.069
Hydroxyethyl starch	16 405	14	1	0.085
Succinylated gelatin	6028	4	1	0.066
Urea-linked gelatin	6151	9	3	0.146
Oxypolygelatin	810	2	1	0.247

substitutes provides useful data on this matter, some details of which are found in Table 2. They classified allergic reactions arbitrarily into four grades according to their severity: grade 1, skin symptoms and/or mild fever reaction; grade 2, measurable, but not life-threatening cardiovascular or respiratory disturbance; grade 3, shock, life-threatening smooth muscle spasm; and grade 4, cardiac and/or respiratory arrest. The incidence of all grades of reaction to succinylated gelatin was low (0.066%) and marginally less than that of Dextran 70 (0.069%) and hydroxyethyl starch (0.085%). The urea-linked preparation was associated with over twice the incidence of anaphylactoid reactions (0.146%) as the succinylated form. The authors pointed out in this article, that the infusion of colloid volume substitutes is associated with fewer allergic reactions than are blood transfusions (0.2–2%) or, for comparison, penicillin (1–5%).

Lundsgaard-Hansen and Tschirren have accumulated considerable data on clinical experience with succinylated gelatin and reported an incidence of anaphylactoid reactions[23] of 0.075%, a figure similar to Ring and Messmer's.[22] The incidence of the more severe reactions (grades 3 and 4) was, however, very low at 0.007%, or about 1:13 400. They suggested that trace contaminants in the gelatin source may have been responsible for the reactions.

Anaphylactoid reactions are usually observed soon after the commencement of the infusion and seem more likely to occur in nonanaesthetised and normovolaemic subjects.[24] The pathophysiology of reactions has not been fully elucidated. Histamine release has been shown to occur and complement may also be activated.[25] Of the two preparations available in the UK, the succinylated solution has been associated with fewer anaphylactoid reactions than the urea-linked product. Since 1981, in an attempt to lessen the amount of histamine released,[26] the manufacturers of the urea-linked product have reduced the amount of cross-linkage which occurs. Whether this modified solution makes a significant clinical difference, remains to be proven.

New generation gelatins are eliminated from the body mainly by glomerular filtration and more than 60% is recoverable in the urine after 24 hours. Studies on the urea-linked preparation using hydroxyproline concentrations which constitute 15% of the product, showed that 90–95% of the total dose is eliminated by one week.[27] The product does not appear to accumulate in patients with renal failure.[28] The metabolism and extravascular storage of the new generation gelatins require further elucidation. The small percentage not recoverable in the urine may be converted by proteases into smaller peptides and amino acids. The distribution of the two gelatin products within the body is shown in Table 3. Dextran 70 and hydroxyethyl starch are included for comparison.

Abnormal haemostasis is a potential problem

Table 3. Distribution of various colloid substitutes 24 hours after intravenous injection into man (after Mishler[29]).

Type of colloid	Plasma (%)	Urine (%)	Extravascular (%)	Overall survival in blood
Urea-linked gelatin	13	71	16	168 hours
Succinylated gelatin	12	62	26	168 hours
Dextran 70	29	38	33	4–6 weeks
Hydroxyethyl starch 450/0.7	38	39	23	17–26 weeks

Table 4. Prices of various colloid solutions.[31]

	Quantity (ml)	Price (£)
New generation gelatins		
Succinylated gelatin (Gelofusine)	500	2.87
Urea-linked gelatin (Haemaccel)	500	3.81
Dextran 70	500	3.82*
Hydroxyethyl starch (Hespan)	500	16.72
Human albumin		
Human albumin 4.5% (National Blood Transfusion Service)	400	24.15
Human albumin 4.3% (Immuno)	400	37.00
Albuminar 5%	500	57.25

* Price varies with manufacturer.

with other colloid plasma substitutes, especially Dextran, where a change in the function of factor VIII decreases platelet aggregability and thrombus stability.[30] The new generation gelatins do not impair haemostasis, apart from a dose-dependent dilution of clotting factors. In contrast to some of the Dextrans, the gelatins now available do not interfere with blood grouping and cross-matching. The inclusion of calcium in the urea-linked preparation may cause citrated blood to clot. It is therefore advisable, when this particular product is used, to flush the infusion with a saline solution before the administration of blood.

Up to 14.5 litres of the succinylated preparation have been administered within a 24-hour period.[24] The tolerance to such volumes suggests that the product has a high dosage ceiling. Prices of various colloids are outlined in Table 4.

Conclusion

Different forms of gelatin have been utilised in intravenous therapy for over half a century and they have become more acceptable lately. Protagonists of the new generation gelatins recommend them as a colloid boost in a variety of clinical situations. They are, however, not available in the USA.

New generation gelatins help to fill the hiatus that exists between crystalloids and blood products. They are relatively inexpensive and freely available, can be used in small or large volumes and may be stored for long periods. They appear to be physiologically inert and are largely excreted unchanged. In hypovolaemic situations, the solutions are useful in the maintenance of plasma expansion because of their macromolecular structure and, in more severe haemorrhage, help to maintain the circulation until blood is available.

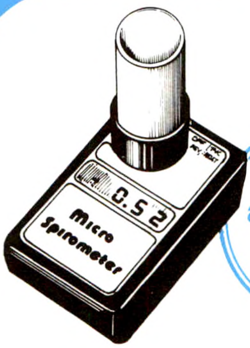
References

1. Twigley AJ, Hillman KM. The end of the crystalloid era? A new approach to peri-operative fluid administration. *Anaesthesia* 1985; **40:** 860–71.
2. Starling EH. On the absorption of fluids from the connective tissue spaces. *Journal of Physiology, London* 1896; **19:** 312–26.
3. Erlanger J, Gasser HS. Hypertonic gum acacia and glucose in the treatment of secondary traumatic shock. *Annals of Surgery* 1919; **69:** 389–421.
4. Bayliss WM. Methods of raising a low arterial pressure. *Proceedings of the Royal Society of Britain* 1916; **80:** 380.
5. Hartmann A, Senn MJE, Nelson MV, Perley AM. The use of acacia in the treatment of edema. *Journal of the American Medical Association* 1933; **100:** 251–4.
6. Studdiford WE. Severe and fatal reactions following intravenous use of gum acacia glucose infusions. *Surgery, Gynecology and Obstetrics* 1937; **64:** 772–84.
7. Dick MW, Warweg E, Andersch M. Acacia in the treatment of nephrosis. *Journal of the American Medical Association* 1935; **105:** 654–7.
8. Hogan JJ. The use of colloidal (gelatin) solutions in shock. *Journal of the American Medical Association* 1915; **64:** 721–6.
9. Jacobson SD, Smyth CJ. Gelatin as a substitute for plasma. Observations on its administration to human beings. *Archives of Internal Medicine* 1944; **74:** 254–7.
10. Greaves RIN. Blood derivatives and blood substitutes. In: Keynes G, ed. *Blood transfusion.* Bristol: John Wright and Sons, 1949: 548.
11. Campbell DH, Koepfli JB, Pauling L, Abrahamson N, Dandliker W, Feigen GA, Lanni F, Le Rosen A. The preparation and properties of a modified gelatin (oxypolygelatin) as an oncotic substitute for serum albumin. *Texas Reports on Biology and Medicine* 1951; **9:** 235–80.

12. Hecht G, Weese H. Periston, ein neuer Blutflüssigkeitsersatz. *Münchener medizinische Wochenschrift* 1943; **90:** 11.
13. Grönwall A, Inglemann B. Untersuchungen uber Dextran und sein Verhalten bei paranteraler Zufuhr. *Acta Physiologica Scandinavica* 1945; **9:** 1–27.
14. Hartman FW, Behrmann VG. The present status of plasma expanders. *Journal of the American Medical Association* 1953; **152:** 1116–20.
15. Evans EI, Rafal HS. Studies on traumatic shock. The treatment of clinical shock with gelatin. *Annals of Surgery* 1945; **121:** 478–94.
16. Nitschmann H, Stoll HR. Gelatin as starting material for the manufacture of plasma substitute preparations. *Bibliotheca Haematologica* 1969; **33:** 55–74.
17. Tourtelotte D, Williams HE. Acylated gelatins and their preparations. *US Patent* 1958; **2:** 827.
18. Schmidt-Thome J, Mager A, Schöne HH. Zur Chemie eines neuen Plasmaexpanders. *Arzneimittelforschung* 1962; **12:** 378–80.
19. Schöne HH. Chemistry and physicochemical characterization of gelatin plasma substitutes. *Bibliotheca Haematologica* 1969; **33:** 78–80.
20. Tourtelotte D, Williams HE. *Recent advances in gelatin and glue research.* New York: Pergamon, 1958.
21. Freeman MK. Fatal reaction to haemaccel. *Anaesthesia* 1979; **34:** 341–3.
22. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; **1:** 466–9.
23. Lundsgaard-Hansen P, Tschirren B. Clinical experience with 120,000 units of modified fluid gelatin. *Developments in Biological Standardization* 1981; **48:** 251–6.
24. Lundsgaard-Hansen P, Tschirren B. Modified fluid gelatin as a plasma substitute. In: Jamieson GA, Greenwalt T, eds. *Blood substitutes and plasma expanders. Proceedings, 9th American Red Cross Annual Scientific Symposium, Washington DC, 1977.* New York: Alan R. Liss, Inc., 1978: 227–57.
25. Lorenz W, Doenicke K, Messmer HJ, Reimann M, Thermann M, Lahn W, Berr J, Schmal A, Dormann P, Regenfuss P, Hamelmann H. Histamine release in human subjects by modified gelatin (Haemaccel) and dextran: an explanation for anaphylactoid reactions observed under clinical conditions? *British Journal of Anaesthesia* 1976; **48:** 151–65.
26. Schöning B, Lorenz W. Prevention of allergoid (cutaneous anaphylactoid) reactions to polygeline (Haemaccel) in orthopaedic patients by premedication with H1- and H2-receptor antagonists. *Developments in Biological Standardization* 1981; **48:** 241–9.
27. Zenkorn D. Intravenous retention, dispersal, excretion and breakdown of gelatin plasma substitutes. *Bibliotheca Haematologica* 1969; **33:** 131–40.
28. Köhler H, Kirch W, Fuchs P, Stalder K, Distler A. Elimination of hexamethylene diisocyanate cross-linked polypeptides in patients with normal or impaired renal function. *European Journal of Clinical Pharmacology* 1978; **14:** 405–12.
29. Mishler JM 4th. Synthetic plasma volume expanders—their pharmacology, safety and clinical efficacy. *Clinics in Haematology* 1984; **13:** 75–92.
30. Bergqvist D. Dextran and haemostasis. A review. *Acta Chirurgica Scandinavica* 1982; **148:** 633–40.
31. *Monthly Index of Medical Specialities* (MIMS), August 1986.

micro Medical

The inexpensive alternative ...



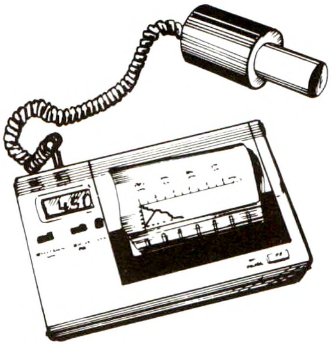
Now available in new format

Micro Spirometer

An inexpensive Spirometer for measurement of the Forced Expired Volume in one second (FEV$_1$) and the Forced Vital Capacity (FVC). The Micro Spirometer's low cost makes it eminently suitable for patient home use and large scale clinical trials.

Pocket Spirometer

The Spirometer for measurement of the FEV$_1$, FVC and Peak Flow. The Pocket Spirometer enables the three most important parameters of Lung Function to be recorded together virtually anywhere.



Printer Spirometer

The Spirometer of choice where a permanent record of test results are required. The Printer Spirometer measures seven Flow-Volume parameters with both Volume-Time and Flow-Volume Curves.

Stand No. 76
Annual Scientific Meeting
Sheffield

Microloop

The complete Flow-Volume System designed for full Spirometry screening featuring real time volume display, patient predicted values and full A4 size report. Microloop is an inexpensive, easy to use and reliable Laboratory Spirometer.

For all your spirometry requirements

Micro Medical Limited
P.O. Box 6, Rochester,
Kent ME1 2AZ ENGLAND
Telephone: Medway (0634) 712290
Telex: 8950511 Ref: 13630001

NOW! A FULL
OXIMETER FOR

- Safe
- Simple
- Reliable
- Accurate

EATURE PULSE ESS THAN £2000.*

INCLUDING SENSOR

- **MOTION ARTIFACT REJECTION SYSTEM**
- **SaO$_2$ PULSE RATE** displays are large and easy to read
- **PULSE BAR GRAPH** shows pulse activity
- **WEIGHS ONLY 8 POUNDS (3.6 KILOS)**
- **FULL RANGE OF EAR, FINGER AND NEO-NATAL SENSORS**

The Novametrix 500 Pulse Oximeter features an exclusive Tele-sat system. Employing wireless telemetry, it allows up to 8 units to be displayed simultaneously on a central monitor.

With Health Service funds in short supply, here's an opportunity to buy a British-made product with advanced technology – at the lowest price.

For an immediate demonstration, contact us today.

Price relates to hospital buying programme.

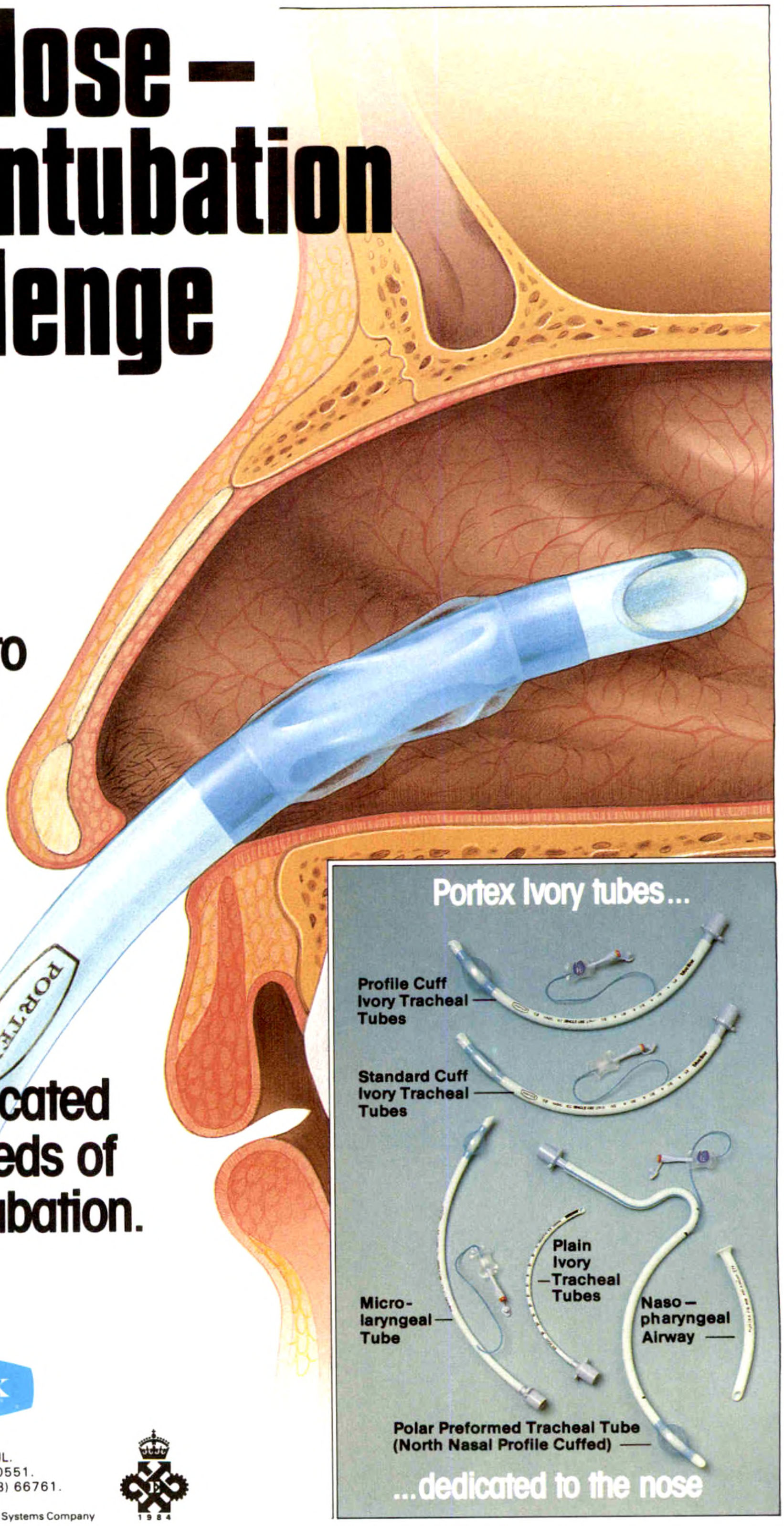
Exclusive Distributor for Britain

LTHIN (UK) LIMITED
4 Vincent Road
Selsey, Chichester, West Sussex PO20 9DH
TEL: (0243) 602607 TELEX: 94012812 ALUKG
FAX: (0243) 607114

althin

The Nose –
The Intubation
Challenge

To avoid damage to the nasal passage it makes sense to choose a soft tracheal tube dedicated to the needs of nasal intubation.


PORTEX
Portex Ivory tubes...
Profile Cuff Ivory Tracheal Tubes
Standard Cuff Ivory Tracheal Tubes
Micro-laryngeal Tube
Plain Ivory Tracheal Tubes
Naso-pharyngeal Airway
Polar Preformed Tracheal Tube (North Nasal Profile Cuffed)
...dedicated to the nose

PORTEX

PORTEX LIMITED
Hythe, Kent, England, CT21 6JL.
Tel: Hythe (0303) 66863 & 60551.
Telex: 96165. Facsimile: (0303) 66761.

sims A Smiths Industries Medical Systems Company

1984

Anaesthesia, 1987, Volume 42, pages 1005–1008

Forum

The morphine sparing effects of diclofenac sodium following abdominal surgery

N. B. A. Hodsman, FFARCS, Senior Registrar, J. Burns, FFARCS, Research Fellow, Glasgow Royal Infirmary, A. Blyth, FFARCSI, Senior Registrar, Stobhill Hospital, G. N. C. Kenny, BSc, MD, FFARCS, Senior Lecturer, Glasgow Royal Infirmary, C. S. McArdle, MD, FRCS, Consultant Surgeon, Glasgow Royal Infirmary, H. Rotman, Clinical Research Executive, Ciba-Geigy Pharmaceuticals.

Summary

A randomised, double-blind placebo controlled study was undertaken to assess the analgesic efficacy of diclofenac. Following major abdominal surgery and 12 hours later, patients received either placebo or diclofenac 75 mg intramuscularly and their cumulative morphine requirements administered by a patient-controlled system over 24 hours were compared. Pain scores were also measured. Arterial blood gases and coagulation studies were assessed pre- and postoperatively. Morphine consumption was significantly greater in the placebo group (59.5 compared to 38.5 mg, $p < 0.01$). Pain scores were significantly lower in the diclofenac group at 4 hours, but not thereafter. Arterial carbon dioxide was significantly increased in the control groups. There was no significant change in platelet count within each group, but a significant difference between the groups ($p < 0.05$).

Key words

Analgesics, narcotic; morphine.
Analgesics, non-narcotic; diclofenac.

The effective management of postoperative pain remains a problem for the anaesthetist and surgeon. Many patients experience severe pain using the conventional regimen of intermittent intramuscular opioids.[1,2] This may be caused by factors such as fear of respiratory depression or addiction with on-demand regimens, which results in irregular administration, fluctuating plasma concentrations and inadequate relief of pain. Furthermore, many patients will not request analgesia unless specifically asked if they are in pain and, in addition, the delay between request and effective plasma concentrations may be as long as 1 hour.[3]

Recent studies have suggested that the addition of non-steroidal anti-inflammatory drugs may reduce opioid requirements, improve pain relief and reduce respiratory depression.[4,5] Diclofenac is a phenylacetic acid derivative with significant analgesic, anti-inflammatory and antipyretic properties. It is a member of the prostaglandin synthetase inhibitor group of drugs and is available in parenteral form. Baroni and his colleagues[6] have demonstrated that diclofenac has an analgesic effect within 30 minutes in 80% of patients when used for postoperative pain relief; in 83% of cases the analgesic effect lasted for more than 4 hours. It has been shown to provide effective pain relief in inflammatory joint disease, renal colic and, more recently, in the control of pain following hip surgery.[7,8]

The aim of this study was to assess the analgesic efficacy of intramuscular diclofenac following major abdominal surgery.

Methods

Patients scheduled to undergo abdominal surgery between the ages of 18–75 years and weight 40–95 kg, were considered eligible for inclusion in this study. Those with manifest respiratory, cardiac, hepatic or renal insufficiency, a history of haemorrhagic diathesis, haematemesis or anticoagulant therapy, or allergy to aspirin, diclofenac or other prostaglandin-inhibiting compounds, were not studied. Patients who had a history of peptic ulceration and were not scheduled to undergo corrective surgery, were also excluded. The study was approved by the hospital ethical committee and all patients gave informed consent.

0003–2409/87/091005 + 10 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

The patients received temazepam 20–40 mg orally as premedication. Anaesthesia was induced with thiopentone and maintained with nitrous oxide, oxygen and halothane or enflurane, with increments of vecuronium or atracurium to provide muscle relaxation. Increments of morphine were administered as required.

Patients were allocated randomly to receive either intramuscular diclofenac 75 mg or placebo, on conclusion of surgery and 12 hours later. Cumulative morphine requirements were assessed using a patient-controlled analgesia system.[9] This allows the patient to relieve pain by self administration of increments of morphine intravenously and provides an accurate method for the determination of opioid requirements. The system was attached to the patient's intravenous line immediately following surgery. The device was programmed to deliver an incremental dose of 0.02 mg/kg with a minimum lock-out interval of 2 minutes between doses. Patients were instructed pre-operatively in the use of the device.

Pain was assessed by visual linear analogue 100-mm horizontal scores at 4, 8, 12 and 24 hours postoperatively. Arterial samples were taken for blood gas analysis pre-operatively and at 24 hours postoperatively. Blood coagulation studies were performed at similar time intervals to determine whether there was any significant thrombocytopenic effect of diclofenac.

Demographic data were analysed using Student's *t*-test. Nonparametric data were analysed by a two-tailed Mann–Whitney *U* test.

Results

Sixty-five patients were entered into the study. There were no significant differences between the groups in age, sex, height, weight or the amount of morphine administered intra-operatively (Table 1). Three patients were subsequently withdrawn from the study and their results were not analysed. Two patients were withdrawn from the diclofenac group, one at 4 hours, the other at 11 hours, because of postoperative bleeding and both required re-operation. Both patients had undergone abdomino-perineal resections of rectum with extensive pelvic dissection due to contiguous organ involvement; the blood loss for both patients during the initial operation was greater than 1500 ml. At re-operation, the blood loss was 2–3 litres for each patient. No obvious bleeding points were found. Coagulation studies in both patients were consistent with the effects of bleeding.

Table 1. Comparison of groups: values expressed as mean (SD).

	Control ($n = 31$)	Diclofenac ($n = 31$)
Age, years	44 (15)	45 (17)
Female:male	18:13	15:16
Weight, kg	65 (13)	67 (13)
Height, cm	167 (9)	167 (9)
Morphine consumption in theatre, mg	12 (3.6)	13.4 (5)

One patient was withdrawn from the placebo group because of inadequate analgesia, despite the fact that she had consumed 99.6 mg morphine in 11 hours. She did not show any signs of respiratory depression but it was felt that the lack of continuous respiratory monitoring precluded continuation of the analgesia system.

The cumulative 24-hour morphine requirements are shown in Table 2 and Fig. 1. The mean 24-hour

Table 2. Twenty-four-hour morphine consumption: values expressed as mean (SEM).

	Control ($n = 31$)	Diclofenac ($n = 31$)
Morphine consumption, mg	59 (5)	38 (4)*

* $p < 0.01$.

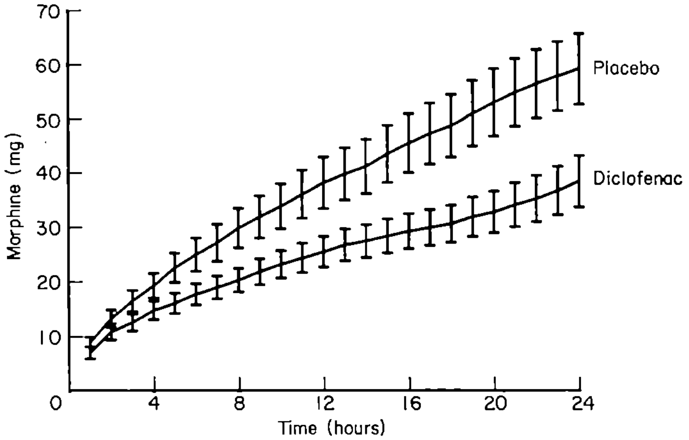


Fig. 1. Cumulative morphine consumptions (mg) for control and diclofenac groups (mean, SD).

Table 3. Linear analogue pain scores: values expressed as mean (SEM).

	Control	Diclofenac
4-hour pain score, mm	40 (4) (n = 27)	23 (4)* (n = 28)
8-hour pain score, mm	35 (6) (n = 19)	25 (5) (n = 24)
12-hour pain score, mm	24 (3) (n = 28)	25 (4) (n = 27)
24-hour pain score, mm	28 (4) (n = 30)	23 (4) (n = 31)

* $p < 0.01$. Patients who were asleep did not complete pain scores. One patient in the control group did not complete the final pain score.

Table 4. Change in arterial carbon dioxide tensions pre- and postoperatively: values expressed as mean (SEM).

	Control (n = 30)	Diclofenac (n = 28)
Pre-operative $Pa\text{CO}_2$, kPa	4.87 (0.07)	4.93 (0.09)
Postoperative $Pa\text{CO}_2$, kPa	5.2 (0.13)	5.1 (0.12)
Increase in $Pa\text{CO}_2$, kPa	0.32 (0.16)*	0.2 (0.13)

* $p < 0.05$. One patient in the control group and three in the diclofenac group refused arterial blood sampling.

morphine consumption of the placebo group was significantly greater than that of the diclofenac group ($p < 0.01$). Visual analogue pain scores at 4 hours were significantly lower in those who received diclofenac ($p < 0.01$; Table 3). There was no significant difference at 8, 12 or 24 hours. There was a small but significant increase in mean arterial carbon dioxide tensions in the control group ($p < 0.05$) but not in the diclofenac group (Table 4). No patient complained of gastrointestinal upset or discomfort associated with the injection.

Table 5. Comparison of platelet counts pre- and postoperatively: values expressed as mean (SEM).

	Control (n = 31)	Diclofenac (n = 27)
Pre-operative platelet count, $\times 10^6$/ml	288 (14)	285 (15)
Postoperative platelet count, $\times 10^6$/ml	296 (19)	257 (13)
Change in platelet count, $\times 10^6$/ml	+8.7 (12)	−28 (9)*

* $p < 0.05$. It was not possible to obtain blood samples in four diclofenac patients.

The results of the coagulation studies are shown in Table 5. The patients in the control group had a mean increase of 8.7×10^6 platelets/ml, whereas there was a mean decrease of 28×10^6 platelets/ml in the diclofenac group. The change in the platelet count within each group was not statistically significant but when the change for the control group was compared with that for the diclofenac group, the difference was significant ($p < 0.05$).

Discussion

This study shows that intermittent intramuscular injections of diclofenac reduce mean postoperative morphine consumption by over one-third. This was associated with significantly reduced pain scores 4 hours after surgery but not at 8, 12 or 24 hours. This suggests that better analgesia was achieved at 4 hours with less morphine consumption.

Patients in the control group had a statistically significant increase in arterial carbon dioxide tension ($p < 0.05$), whereas those who received diclofenac showed a smaller increase which was not significant. The increase was not clinically significant in either group but the result supports the findings of an earlier study which showed that combination therapy of opioid and a non-steroidal anti-inflammatory drug was associated with less respiratory depression.[5]

Two patients were withdrawn from the study because they required re-operation; both had received diclofenac. It seems likely that the postoperative bleeding was due to the extensive dissection, the extent of intra-operative blood loss and the presence of a large raw area. Perhaps diclofenac should not be administered to patients in whom extensive dissection is required until more detailed studies of the antiplatelet effect have been completed.

There was no significant difference in platelet count pre- and postoperatively within each group. The difference in the change in platelets between the two groups was numerically significant but is probably not clinically relevant.

The results of this study show that intermittent intramuscular diclofenac following abdominal surgery has significant morphine sparing properties and reduces the possibility of postoperative respiratory depression. It would appear, therefore, that diclofenac in combination with an opioid has an important role to play in the management of uncomplicated abdominal surgery.

Acknowledgments

We wish to thank all our surgical, anaesthetic and nursing colleagues for their assistance with this study. Diclofenac was supplied by Ciba–Geigy.

References

1. Nayman J. Measurement and control of postoperative pain. *Annals of the Royal College of Surgeons of England* 1979; **61**: 419–26.
2. Tamsen A. Comparison of patient-controlled analgesia with constant infusion and intermittent intramuscular regimes. In: Harmer M, Rosen M, Vickers MD, eds. *Patient-controlled analgesia*. London: Blackwell Scientific Publications, 1985: 111–25.
3. Graves DA, Foster TS, Batenhorst RL, Bennett RL, Baumann TJ. Patient-controlled analgesia. *Annals of Internal Medicine* 1983; **99**: 360–6.
4. Reasbeck PG, Rice ML, Reasbeck JC. Double-blind controlled trial of indomethacin as an adjunct to narcotic analgesia after major abdominal surgery. *Lancet* 1982; **2**: 115–8.

5. Gillies GWA, Kenny GNC, Bullingham RES, McArdle CS. Morphine sparing effect of ketorolac tromethamine, a new parental non-steroidal anti-inflammatory agent, following abdominal surgery. *Anaesthesia* 1987; **42:** 727–31.
6. Baroni L, Grossi E, Trombetta N. Indagine multicentrica sull'impegio del diclofenac iniettabile negli stati dolorosi: un'analisi dei dati clinici relativi a 1873 pazienti. *Clinica Terapeutica* 1983; **106:** 447–56.
7. Hetherington JW, Philip NH. Diclofenac sodium versus pethidine in acute renal colic. *British Medical Journal* 1986; **292:** 237–8.
8. Lindgren U, Djupsjo H. Diclofenac for pain after hip surgery. *Acta Orthopaedica Scandinavica* 1985; **56:** 28–31.
9. Gillies GWA, Kenny GNC, McArdle CS. A standard microcomputer linked to a volume-controlled infusion pump for patient-controlled analgesia research. *Journal of Medical Engineering and Technology* 1986; **10:** 55–7.

Anaesthesia, 1987, Volume 42, pages 1008–1012

The control of intra-ocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique

M. A. Abbott,* FFARCS, Senior Registrar, The Research Department of Anaesthetics, The Royal College of Surgeons of England and St Peter's Hospitals, London WC2, J. R. Samuel, FFARCS, Consultant, Moorfields Eye Hospital, High Holborn, London WC2.

Summary

A technique of rapid sequence induction of anaesthesia for use in patients with penetrating eye injuries is described. This utilises a three maximal breaths method of pre-oxygenation, the intravenous injection of thiopentone and high dose vecuronium (0.2 mg/kg). Using the loss of eyelash reflex as the starting point for timing, all patients were intubated after 60 seconds without coughing and bucking. No postintubation increases in intra-ocular pressure were seen in 70% of patients and in no patient did the increase in intra-ocular pressure exceed 5 mmHg. After 3 minutes of apnoea, the minimum haemoglobin oxygen saturation was 94% with a mean value of 97.6%.

Key words

Anaesthetic techniques; pre-oxygenation.
Neuromuscular relaxants; vecuronium.

The ideal method of induction of anaesthesia in patients with penetrating eye injuries has always been a matter of controversy because of the risk of vitreous loss. The recent paper by Morton and Hamilton[1] suggested that a combination of vecuronium and alfentanil would produce optimal conditions for intubation in patients with open eye injuries and a potentially full stomach. It is obviously important to know the effect of this technique on the intra-ocular pressure (IOP). This study was undertaken with the purpose of showing the contribution that each drug makes towards the production of these optimal conditions.

Both Morton and Hamilton and ourselves have used a modification of a technique described by Holloway[2] in 1980 but, in the present study, emphasis was placed on both the measurement of IOP and the prevention of hypoxia if difficult intubation conditions should be encountered.

Method

Twenty patients scheduled to undergo elective ophthalmic surgery were studied. The patients had to satisfy the following criteria before they were admitted to the trial. Only patients who were in ASA physical assessment groups 1 or 2, did not suffer from glaucoma or abnormal corneal conditions and were not taking any drugs that might obtund the reflex autonomic responses to intubation, were admitted to the tria Research ethics committee approval was obtained and all patients gave their written consent to the procedure.

---

* Present address: The Anaesthetic Unit, The London Hospital Medical College, Whitechapel, London E1 1BB.

Anaesthetic technique. Premedication consisted of papaveretum 0.2 mg/kg and hyoscine 0.004 mg/kg intramuscularly, one hour pre-operatively. A 21-G Y-Can cannula was inserted and the patient pre-oxygenated using the three maximal breaths technique and then asked to breathe normally with the anaesthetic mask still applied. Vecuronium 0.2 mg/kg was administered intravenously and this was immediately followed by thiopentone 4–5 mg/kg. Cricoid pressure was applied as consciousness was lost and the patient was allowed to remain apnoeic. The patient was intubated when clinically indicated (see Observations). Anaesthesia was maintained with supplements of thiopentone 25–50 mg every 60 seconds until 3 minutes had elapsed from the time of induction. From then on, an anaesthetic technique most appropriate for the intended operation was commenced.

Observations. On arrival in the anaesthetic room, baseline recordings of blood pressure and pulse were taken using blood pressure (Dinamap) and ECG monitors. The haemoglobin oxygen saturation was monitored using a Biox IV oximeter and an earlobe probe. These measurements were repeated after pre-oxygenation and then at 60-second intervals from the time of induction. This timing started at the observation of the loss of eyelash reflex. The IOP in the nonoperative eye was determined by the ophthalmologist using a Perkins applanation tonometer. The IOP was measured just prior to pre-oxygenation and then again within one minute of intubation.

The first assessment of intubation conditions was made at 60 seconds from the loss of eyelash reflex and then at 30-second intervals as required. Tracheal intubation was attempted only if the anaesthetist felt that a smooth intubation could be achieved.

The reaction to intubation was then recorded as: (1) excellent, a fully relaxed jaw with fully abducted vocal cords but no cough; (2) adequate, either a partly relaxed jaw or partly abducted vocal cords but no cough; or (3) poor, partly relaxed jaw with partly abducted cords or a cough.

Neuromuscular blockade was assessed by stimulating the ulnar nerve with a Bard 750 peripheral nerve stimulator set in the train-of-four mode. The presence or absence of the adductor pollicis twitches was ascertained by visual and tactile observation. Supplements of vecuronium were administered during the more lengthy procedures. Residual neuromuscular blockade was reversed with neostigmine in appropriate doses when the third twitch was observed.

Table 1. Intra-ocular pressure (IOP) changes, mmHg: values expressed as mean (SD).

IOP, mmHg		Maximum increase in IOP after intubation	Percentage of postintubation IOPs greater than pre-induction level
Pre-induction	Post-intubation		
15.4 (4.5), range 7–24	13.9 (4.8), range 8–23	+5 mmHg	30%

Results are expressed as mean (SD) values. Statistical analysis was applied to the intra-ocular pressure changes using Student's *t*-test.

Results

Twenty patients, of whom 13 were male, with a mean age of 54.1 years (SD 15.5) and a mean weight of 72.9 kg (SD 16.1), were admitted to the trial. The intra-ocular pressure changes associated with induction of anaesthesia and tracheal intubation are shown in Table 1. In those patients who had a postintubation increase in IOP above the baseline value, the maximum seen was 5 mmHg with a mean of 3.3 mmHg. The mean decrease in IOP seen after intubation did not reach a point of significance.

Sixty percent of patients had excellent, and 40% had adequate intubation conditions (see Methods). No patient coughed or bucked but three patients exhibited minimal, transient diaphragmatic movements that lasted for less than 10 seconds. These three patients had postintubation intra-ocular pressures close to their resting levels (pressure decreased by 4 and 5 mmHg respectively in two patients, and increased by 4 mmHg in one).

All patients exhibited a marked haemodynamic response to intubation, as seen in Fig. 1. Postintuba-

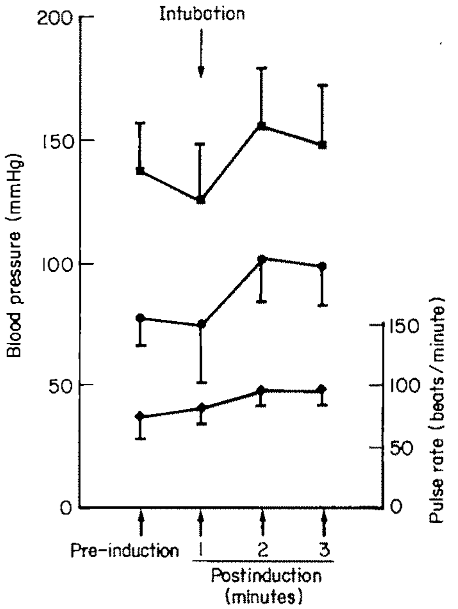


Fig. 1. The haemodynamic changes associated with the induction of anaesthesia and tracheal intubation. ■, Systolic pressure; ●, diastolic pressure; ◆, pulse rate (means of all patients).

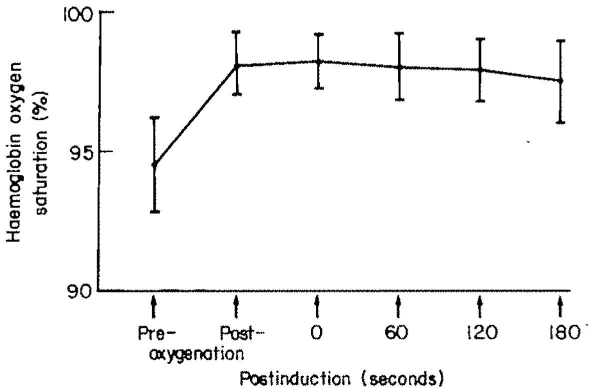


Fig. 2. The effect of three maximal breaths pre-oxygenation on haemoglobin oxygen saturation during apnoeic anaesthesia (means of all patients).

Table 2. Reappearance time of train-of-four twitches, minutes: values expressed as mean (SD).

	With inhalational supplements	Without inhalational supplements
2nd twitch	62.3 (11.6), range 45–86	40
3rd twitch	69.7 (13.7), range 49–95	42

tion, the maximum increase in systolic arterial pressure seen in any patient was 74 mmHg.

The effects of pre-oxygenation and postinduction apnoea on the haemoglobin oxygen saturation levels are shown in Fig. 2. The minimum value before pre-oxygenation was 92% and afterwards, 97%. The lowest reading after 3 minutes of apnoea was 94%.

The reappearance times of the second and third muscle twitches when using train-of-four nerve stimulation are shown in Table 2. All but one of the patients received inhalational supplements of either enflurane or halothane. There was good clinical reversal of the neuromuscular blockade in all patients when neostigmine was administered even if they had received supplementary doses of vecuronium.

Discussion

The anaesthetic management of patients with penetrating eye injuries and a full stomach, can be complicated by the pulmonary aspiration of gastric contents. A rapid sequence induction using suxamethonium offers the best method to prevent pulmonary aspiration but this may be at the expense of further ocular damage due to a sudden increase in IOP.

It is usual to wait until the stomach has emptied (either naturally, or accelerated by the use of metoclopramide) and to use a non-depolarising muscle relaxant anaesthetic technique but there may be occasions where immediate surgery is required to the affected eye or to other traumatised organs. If this is the case, the risks of pulmonary aspiration have to be balanced against factors that may lead to further intra-ocular damage and loss of vitreous, and possible total loss of ocular function. The use of self-taming techniques, pretreatment with small doses of competitive muscle relaxants or diazepam has proved to be ineffective in consistently obtunding the increase in IOP that follows the use of suxamethonium. This problem has been comprehensively reviewed by Murphy.[3]

Ideally, if a muscle relaxant is to replace the use of suxamethonium in rapid sequence induction, the clinical time of onset should not differ markedly from that of suxamethonium. Studies by Marshall Barr and Thornley,[4] and also by Hey,[5] showed a mean time of about 45 seconds between loss of eyelash reflex and intubation when suxamethonium was used. However, this period of time ranged up to 120 seconds in some of the patients.

On the other hand, Casson and Jones[6] have shown that increasing the vecuronium dosage above 0.15 mg/kg has little effect on foreshortening the onset time to full neuromuscular blockade. In patients premedicated with diazepam, Mirakhur *et al.*[7] found that at 60 seconds, vecuronium in a dose of 0.2 mg/kg had little advantage over 0.15 mg/kg in terms of adequate intubation conditions (only 60% were graded as satisfactory or better). However, Lennon *et al.*[8] have shown that clinically adequate intubation conditions could be obtained 60 seconds after the injection of vecuronium 0.25 mg/kg in unpremedicated patients. Therefore, we decided to administer a dose of 0.2 mg/kg vecuronium to opiate-premedicated patients in order to determine whether clinically useful intubation conditions could be consistently produced at 60 seconds without a significant elevation in IOP on intubation.

The results show that at 60 seconds, just over 50% of our patients had excellent intubation conditions and the remainder were adequate. This lack of reflex muscular response to intubation may be due, in part, to the analgesic and sedative effects of the premedication combined with the reflex-depressing action of thiopentone, rather than to pure neuromuscular blockade. Nevertheless, our regimen produced clinically dependable intubation conditions.

Sudden changes in blood pressure can override the autoregulatory mechanisms in the eye and lead to a transient elevation in IOP. All the patients exhibited a marked haemodynamic response to the stimulus of tracheal intubation but a consistent increase in IOP above the resting level was not seen in every patient. Morton and Hamilton expanded on the work of Black *et al.*,[9] who showed that alfentanil attenuates the hypertensive response to intubation. However, since they did not measure the effect of their anaesthetic technique on the IOP, it may be premature to advocate its use in anaesthesia for penetrating eye injuries.

A comparison of the pre-induction and post-intubation IOP shows a decrease in the observed values (although this was not statistically significant). Similar results were demonstrated by Sia and Rashkovsky[10] and others.[11] There was an IOP increase in 30% of our patients after intubation but the maximum seen in any one patient was 5 mmHg (mean 3.3 mmHg). These elevations in postintubation intraocular pressure are transient in nature and start to decrease within one to two minutes.[12] There is no extra-ocular component to these pressure changes when vecuronium is used. This contrasts with the prolonged elevation seen when suxamethonium is administered.

The use of tubocurarine will produce a decrease in IOP[11] but its slow onset makes it an unsuitable agent for rapid intubation. Pancuronium has little effect on IOP but increasing the initial dose in an attempt to foreshorten the time to adequate intubation conditions, will produce a prolonged period of irreversible neuromuscular blockade.[13] When equipotent doses of vecuronium and atracurium are compared, there is little to choose between them in terms of speed of onset or time to the production of clinically useful intubation conditions. However, the administration of high dose atracurium can result in the production of marked haemodynamic depression.[8] This may be deleterious in the traumatised patient. Scott *et al.*[14] showed that this could be prevented by injecting the atracurium over a period of 75 seconds; the administration of atracurium in this fashion, would render its use unsuitable for a rapid sequence technique.

Another cause of increased IOP is hypercapnia.[15] Carbon dioxide retention occurs during the period of apnoea prior to tracheal intubation and the commencement of artificial ventilation but this is counteracted by the hyperventilation which takes place during the three maximal breaths pre-oxygenation. After 3 minutes of apnoea, $P\text{aco}_2$ increases by approximately 1.2 kPa and, even if the patient is assumed to be normocarbic at the induction of anaesthesia, IOP will only increase during this time by approximately 1.5 mmHg above its resting level.[16]

Hypoxia is an ever-present risk during the induction of anaesthesia, especially when difficult intubation conditions are met unexpectedly during a crash induction. The three maximal breaths method of pre-oxygenation, as described by Drummond and Park,[17] is effective in rapidly producing a pulmonary reserve of oxygen. The lowest oxygen saturation seen in our patients was 94% even after 3 minutes of apnoea. However, if the patient suffers from injuries that inhibit the ability to take deep breaths or prevent the tight application of the anaesthetic mask to the face, normal pre-oxygenation over 2 or 3 minutes should produce the same end result. With this proviso, the three maximal breaths technique produces good levels of oxygenation for sufficient time that, if difficulties in intubation are encountered, further attempts at intubation can be undertaken without recourse to manual ventilation.

Neuromuscular monitoring of these patients revealed a mean third twitch reappearance time of 69.7 minutes. The reappearance time ranged up to 95 minutes. As ophthalmic procedures for penetrating eye injuries are intricate and thus prolonged, there should be little likelihood of a situation where reversal of the neuromuscular blockade is unsuccessful. However, it should be noted that the neuromuscular blocking activity of vecuronium wears off fairly rapidly and, as only a light anaesthetic using low concentrations of inhalational agents is required for this type of ophthalmic surgery, it would be prudent to commence early monitoring of neuromuscular blockade if the potentially harmful effects of sudden patient movement on the open eye are to be avoided.

Acknowledgments

The authors thank Professor J.P. Payne for his constructive criticism of this paper. We would also like to express our gratitude to the ophthalmic surgeons of Moorfields Eye Hospital who measured the intraocular pressures and Messrs Brooks and Zinsa for their technical assistance. Organon kindly donated the vecuronium and Ohmeda loaned the Biox IV oximeter.

References

1. MORTON NS, HAMILTON MB. Alfentanil in an anaesthetic technique for penetrating eye injuries. *Anaesthesia* 1986; **41:** 1148–51.
2. HOLLOWAY KB. Control of the eye during general anaesthesia for intraocular surgery. *British Journal of Anaesthesia* 1980; **52:** 671–9.
3. MURPHY DF. Anesthesia and intraocular pressure. *Anesthesia and Analgesia* 1985; **64:** 520–30.
4. MARSHALL BARR A, THORNLEY BA. Thiopentone and suxamethonium crash induction: an assessment of the potential hazards. *Anaesthesia* 1976; **31:** 23–9.

5. HEY VMF. Relaxants for endotracheal intubation. A comparison of depolarising and non-depolarising neuromuscular blocking agents. *Anaesthesia* 1973; **28:** 32–6.
6. CASSON WR, JONES RM. Vecuronium induced neuromuscular blockade. *Anaesthesia* 1986; **41:** 354–7.
7. MIRAKHUR RK, FERRES CJ, CLARKE RSJ, BALI IM, DUNDEE JW. Clinical evaluation of Org NC45. *British Journal of Anaesthesia* 1983; **55:** 119–24.
8. LENNON RL, OLSON RA, GRONERT GA. Atracurium or vecuronium for rapid sequence endotracheal intubation. *Anesthesiology* 1986; **64:** 510–13.
9. BLACK TE, KAY B, HEALY TEJ. Reducing the haemodynamic responses to laryngoscopy and intubation. *Anaesthesia* 1984; **39:** 883–7.
10. SIA RL, RASHKOVSKY OM. Org NC45 and intraocular pressure during anaesthesia. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 219–21.
11. AL-ABRAK MH, SAMUEL JR. Effects of general anaesthesia on the intraocular pressure in man. Comparison of tubocurarine and pancuronium in nitrous oxide and oxygen. *British Journal of Ophthalmology* 1974; **58:** 806–10.
12. BADRINATH S, VAZEERY AK, IVANKOVICH AD. Effect of vecuronium on intraocular pressure. *Anesthesia and Analgesia* 1986; **65:** S10.
13. BROWN EM, KRISHNAPRASAD D, SMILER BG. Pancuronium for rapid induction technique for tracheal intubation. *Canadian Anaesthetists' Society Journal* 1979; **26:** 489–91.
14. SCOTT RPF, SAVARESE JJ, BASTA SJ, EMBREE P, ALI HH, SUNDER N, HOAGLIN DC. Clinical pharmacology of atracurium given in high dose. *British Journal of Anaesthesia* 1986; **58:** 834–8.
15. SAMUEL JR, BEAUGIÉ A. Effect of carbon dioxide on the intraocular pressure in man during general anaesthesia. *British Journal of Ophthalmology* 1974; **58:** 62–7.
16. SMITH RB, AASS AA, NEMOTO EM. Intraocular and intracranial pressure during respiratory alkalosis and acidosis. *British Journal of Anaesthesia* 1981; **53:** 967–72.
17. DRUMMOND GB, PARK GR. Arterial oxygen saturation before intubation of the trachea. *British Journal of Anaesthesia* 1984; **56:** 987–93.

Anaesthesia, 1987, Volume 42, pages 1012–1014

Tracheal tubes in neuroanaesthesia. Nylon reinforced latex rubber tracheal tubes*

P. J. Wright, FFARCS, Consultant, J. V. B. Mundy, FFARCS, Senior Registrar, Department of Anaesthetics, Royal Hallamshire Hospital, Sheffield S10 2JF.

Summary

An exercise in quality assurance during neuroanaesthetic procedures identified uncontrolled re-use of armoured latex rubber tracheal tubes as a risk factor associated with equipment failure. We recommend that such tubes should be used once only. Alternatively, tubes made from more stable materials, such as polyvinyl chloride and silicone rubber, are available for clinical evaluation.

Key words

Complications; accident.
Equipment; tubes, tracheal.

The purpose of an armoured tracheal tube is to protect the airway when compression or kinking might occur and result in respiratory obstruction. Any form of equipment failure related to the tracheal tube represents a great disadvantage because of the difficult nature of the procedures for which such tubes are used. There have been many reports of armoured tracheal tubes causing respiratory obstruction$^{1-17}$ but the risk of this type of tube has not been quantified *in vivo*.

Method

The hospital's existing stock of 350 armoured latex tubes supplied by Eschmann Bros & Walsh Ltd, and Leyland Medical, were checked for faults of any kind. In addition to the routine inspection before use, the tubes were inflated inside the barrel of a 20-ml syringe to check for internal herniation or asymmetrical inflation of the cuff. Any faulty items were discarded. Used tubes were cleaned with soapy water and immersed in activated glutaraldehyde solution for 20 minutes. Stock was rotated as frequently as possible to avoid excessive re-use. Adult neurosurgical patients were intubated orally under direct vision using a lubricated malleable introducer with a size 8.0 mm (female) or 9.0 mm (male) tracheal tube. The cuffs were inflated with the minimum amount of air necessary to provide an effective seal, and the tubes secured with plastic adhesive strapping. Patients were positioned carefully to avoid extreme flexion of the neck, or pressure on the face, and access to the tube and its connexions assured. Expired minute volume, airway pressure on inflation and end tidal carbon dioxide were monitored continuously and any malfunction of the tracheal tube recorded. Troublesome tracheal tubes were retained for inspection and their type recorded.

---

* Some of the results in this paper were presented to the Neuroanaesthetists' Travelling Club at the National Hospital, Queen Square, London on 10 May 1986.

Results

Two hundred of the stock tubes were found to be unused; the rest had been used at least once. Altogether, 443 patients were studied in a wide variety of positions common to neurosurgery. A total of 63 tubes were rejected as hazardous by the anaesthetist, either prior to use or because of failure during the operation; this gives an overall failure rate of 14%. The most common cause for rejection was asymmetrical cuff inflation, usually detected prior to intubation; this occurred with 38 tubes. In one patient there was complete respiratory obstruction which necessitated re-intubation. Tracheal cuff deflation occurred on 17 occasions and was detected by a decrease in expired minute volume and an increase in end tidal carbon dioxide. Re-intubation was required in two of these patients. Internal herniation of the cuff into the lumen of the tube occurred twice; this caused a leak at first, and then respiratory obstruction with increased airway pressure when more air was added to the cuff. Both patients had to be re-intubated. On two occasions the tracheal tube was found to be too short for the patient, which resulted in substitution, and on four occasions the cuff failed to deflate because of debris in the pilot tubing. A total of seven patients required re-intubation during this study, three of whom had been subjected to airway obstruction as a result of equipment failure. In each case the failure was clearly due to the tracheal tube, and the defects could be reproduced *in vitro*. All the tubes found to be substandard had been used more than once, and both types of manufacture were equally represented.

Discussion

We were surprised by the high failure rate experienced with these tracheal tubes, despite the fact that much of the stock was of an unknown age, since all of the tubes had been rigorously tested prior to the start of the study. The instability of latex rubber is well known and the deleterious effects of re-sterilising rubber are well documented.[18] Our results are in agreement with those of other workers, who have experienced asymmetrical cuff inflation,[9,19] internal herniation of the cuff[3,5–7,10,12,14–16] and failure of the cuff to deflate.[19] In addition, we have identified leaking cuffs as a relatively common fault.

The nylon reinforced latex tube was developed as a result of war-time shortage of steel and vulcanised rubber,[20] at a time when re-sterilisation was the only economic solution. Our results show that the price paid for this economy is a high failure rate, which exposes the patient to the risk of airway obstruction and re-intubation during a surgical procedure, even when the tubes are rigorously tested for safety prior to use. Quality assurance studies can be carried out under normal clinical conditions where randomised controlled clinical trials are thought to be unjustified. Once the nature of the problem has been quantified there are at least two possible solutions. Firstly, to use the tracheal tubes once only, and then to discard them. This solution does not take into account the likely deterioration of latex rubber in storage. Secondly, armoured tracheal tubes made of more stable compounds are available for clinical evaluation.

Acknowledgments

We thank Mrs J. Willis for preparation of the manuscript and Mr W. Bembridge, SODA and Mr D. Bywater, ODA for their help in collecting the data for this study. Our thanks are also due to our neurosurgical colleagues for their continuing cooperation.

References

1. Adamson DH. A problem of prolonged oral intubation: case report. *Canadian Anaesthetists' Society Journal* 1971; **18:** 213–4.
2. Burns THS. A danger from flexometallic endotracheal tubes. *British Medical Journal* 1956; **1:** 439–40.
3. Catane R, Davidson JT. A hazard of cuffed flexo-metallic endotracheal tubes. *British Journal of Anaesthesia* 1969; **41:** 1086.
4. Cohen DD, Dillon JB. Hazards of armoured endotracheal tubes. *Anesthesia and Analgesia* 1972; **51:** 856–8.
5. Criado A, Horno R, Gómez-Arnao J, Laiño J, Avello F. Obstrucciones agudas del tubo endotraqueal. *Revista Espanola de Anestesiologia y Reanimacion* 1982; **29:** 40–1.
6. Forrester AC. Mishaps in anaesthesia. *Anaesthesia* 1959; **14:** 388–99.
7. Jacobson J. A hazard of armoured endotracheal anesthesia. *Anesthesia and Analgesia* 1969; **48:** 37–41.
8. Kohli MS, Manku RS. Reinforced endotracheal tube—diversion of air from cuff balloon producing obstruction. *Anesthesiology* 1966; **27:** 513–4.
9. Mirakhur RK. Airway obstruction with cuffed armoured tracheal tubes. *Canadian Anaesthetists' Society Journal* 1974; **21:** 251–3.
10. Mittag G. Vorteile, Fehlar und Gefahren der Endotrachealnarkose. *Zeitschrift für Laryngologie, Rhinologie, Otologie und ihre Grenzgebeite* 1956; **35:** 569–76.
11. Munson ES, Stevens DS, Redfern RE. Endotracheal tube obstruction by nitrous oxide. *Anesthesiology* 1980; **52:** 275–6.

12. Ng TH, Kirimli BI. Hazards in use of anode endotracheal tube: a case report and review. *Anesthesia and Analgesia* 1975; **54:** 710–4.
13. Ohn K, Wu W. Another complication of armoured endotracheal tubes. *Anesthesia and Analgesia* 1980; **59:** 215–6.
14. Pérez Guillermo F, Alvarez Ossorio R, Alvarez Gómez JA, Lozano Tonkin E, López López H, Díaz Cayuela A, Bernal García G. Obstrucción respiratoria producida por tubos endotraqueales de látex reforzados. *Revista Espanola de Anestesiologia y Reanimacion* 1978; **26:** 503–10.
15. Robbie DS, Pearce DJ. Some dangers of armoured tubes. *Anaesthesia* 1959; **14:** 379–85.
16. Rouco Martinez I, Catalá Puigbó E, Baxarias Gascón P. Hernia interna en los tubos endotraqueales anillados de látex. *Revista Espanola de Anestesiologia y Reanimacion* 1984; **31:** 208–10.
17. Rumpf G. Ungenwöhnlicher Narkosezwischenfall. *Zeitschrift für Laryngologie, Rhinologie, Otologie und ihre Grenzgebeite* 1957; **36:** 555–6.
18. Stark DCC, Pask EA. Central sterile supply of endotracheal tubes. *Anaesthesia* 1962; **17:** 195–207.
19. Hedden M, Smith RBF, Torpey DJ. A complication of metal spiral imbedded latex endotracheal tubes. *Anesthesia and Analgesia* 1972; **51:** 859–62.
20. Sanders RD. New endotracheal instruments. *Anesthesiology* 1947; **8:** 57–61.

DO YOU NEED A RELIABLE VENTILATOR CIRCUIT READY FOR USE DAY OR NIGHT?

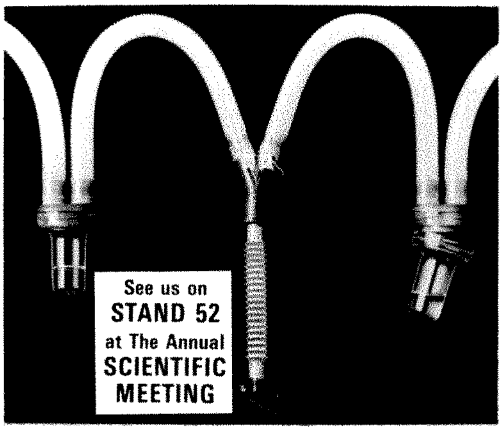
Then we have the answer . . .

Disposable ventilator and anaesthetic circuits pre-assembled ready for immediate use.

- *Eliminate the fear of cross infection*
- *Cut out costly time-consuming sterilisation*
- *Circuits may be custom built to suit your own specific requirements*
- *All connector fittings are safe and secure, manufactured to meet BS3849 specifications*
- *And GMP registration gives you the assurance of high quality*

Reliability combined with cost-effectiveness, it must make sense

REMEMBER IN HEALTH CARE – QUALITY COUNTS.



See us on
STAND 52
at The Annual
SCIENTIFIC MEETING

Intersurgical
COMPLETE RESPIRATORY SYSTEMS

Crane House Gould Road Twickenham Middlesex
England TW2 6RS Tel 01-755 1477 Telex 8953147 INTERS G

RING FOR SAMPLE 01-755 1477

University of London
ROYAL POSTGRADUATE MEDICAL SCHOOL
Hammersmith Hospital
in association with Janssen Pharmaceutical Limited
announces

"A Symposium on Anaesthesia for Day Case Surgery"

Thursday, 29th October, 1987
0930-1700 hours
at the
Hammersmith Hospital, Ducane Road, London

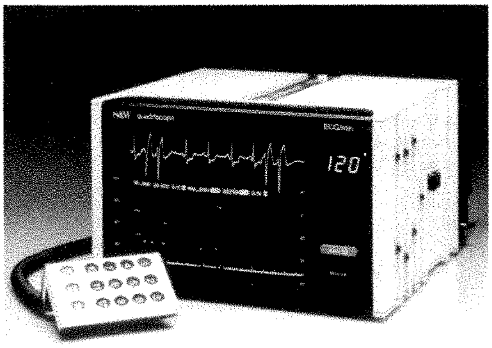
This symposium is intended particularly for Anaesthetists and others interested in the management of day case surgical units.

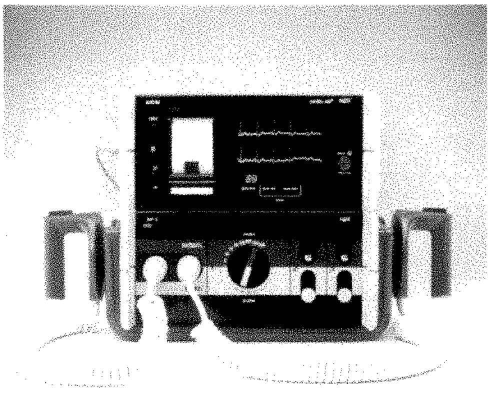
The following topics will be included in the programme:

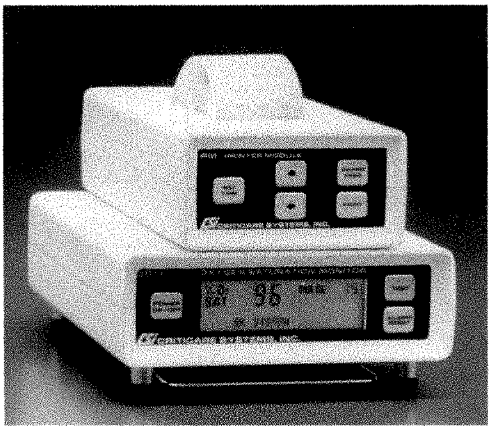
- *the set-up and management of day surgery units,*
- *intravenous anaesthetic agents for day case surgery,*
- *regional anaesthetic techniques for day case surgery.*

For further information please contact Ms. Judith Alexander, Conference Co-ordinator, Janssen Pharmaceutical Limited, Grove, Wantage, Oxon OX12 0DQ. Telephone: Wantage (02357) 2966.

Simonsen & Weel care... about Anaesthesia.







Monitoring for the Anaesthetist

The all new Quadriscope allows three blood pressure waveforms, together with ECG to be displayed simultaneously. A variety of add-on modules means that the Quadriscope can be configured to meet your exact requirements. The Quadriscope is one monitor in the extensive range now offered by Simonsen & Weel for the Anaesthetist, from the ultra simple Diascope 1 and the more comprehensive Diascope 2 range to System 8000 Quadriscope, Simonsen & Weel care about Anaesthesia.

Resuscitation

A comprehensive range of defibrillators including the Defi 2 and the Cardio-Aid family form the basis of this tried and proven range. A variety of resuscitation trollies featuring Simonsen & Weel defibrillators are available to suit most requirements. In addition to defibrillators, Simonsen & Weel have more recently introduced the unique Zoll Non-Invasive Cardiac Pacemaker.

Pulse Oximetry for the Anaesthetist

The latest Criticare oxygen saturation monitor, gives a clear continuous display of $\%O_2$ Saturation and pulse rate, combined with an adjustable alarm limit. This portable unit is extremely versatile and has a variety of sensors available, enabling finger, ear, nasal, forehead and other monitoring sites to be used. Also available is an optional IV pole mount for convenient placement.

Simonsen & Weel Ltd.
Ruxley Corner, Sidcup, Kent DA14 5BL.
Tel: 01-309 0433. Telex: 896328.

S&W

Anaesthesia, 1987, Volume 42, pages 1015–1025

Correspondence

Hallucinations after anaesthesia 1015
E.L. Lloyd, FRCPE, FFARCS
Nerve blocks for hip surgery 1016
A.S.C. Rice, MB, BS and C. Pither, FFARCS
B.E. Smith, FFARCS and A. Allison, FFARCS 1016
Repeated use of halothane 1017
R.R. Macmillan, FFARCS and L.J. Colville, FFARCS
A basic problem at cardiac arrests 1018
S.M. Dumont, FFARCS and S. Mousdale, FFARCS
Nomenclature of circle absorption breathing systems 1018
P.J. Horsey, FFARCS
A. Twigley, FFARCS, M.K. Chakrabarti, BSc, MPhil and J.G. Whitwam, PhD, FRCP, FFARCS 1018
A test for breathing systems 1019
C.M.S. Cooper, MB, BS
Shelf-life of sodium citrate (0.3M) 1019
R. Burgess, FFARACS and J. Wrobel, FFARACS
Prolonged neuromuscular blockade in an infant 1020
J.F. Sinclair, FFARCS, G.A. Malcolm, DCH, J.B.P. Stephenson, FRCPaed and D. Halworth, FFARCS
Priming with vecuronium in obstetrics 1021
S. Cherala, MD, D. Eddie, MD, M. Halpern, MD and K. Shevde, MD
Pain-free intravenous injections 1021
R. Porteous, FFARCS
Unexpected difficult intubation 1021
S.W. Millar, FFARCS
Kinked pilot tube 1022
J. Tanski, MB, BCh, DA and R.H. James, FFARCS
Early textbooks on anaesthesia 1022
O. Secher, FFARCS
Beta blockade and nitroprusside 1022
N.R. Coad, FFARCS
D.L. Simpson, FFARCS 1023
Epidural lavage for extensive epidural suppuration 1023
E. Cardan, MD and M. Nanulescu, MD
Postoperative complications of dystrophia myotonica 1023
D. Zuck, FFARCS
J.K. Moore, FFARCS and A.P. Moore, MRCP 1024
Early retirement and morbidity 1024
A.K. Adams, FFARCS
R. Hutchinson, FFARCS 1024
R.I. Keen, FFARCS and R. McNamee, MSc, PhD 1024
Relative potency of propofol and thiopentone 1025
B. Kay, FFARCS
SI units, Newtons and apples 1025
J.G. Rye, MRCS, LRCP
Leak detection with a capnograph 1025
D.G. Martin, MRCP, FFARCS

Hallucinations after anaesthesia

This is a report of an abnormal response after propofol.

A 40-year-old patient was admitted as a day case for a minor gynaecological procedure; no premedication was given. Induction was with propofol 200 mg and anaesthesia was maintained with nitrous oxide, oxygen and halothane using spontaneous ventilation via a facemask. The anaesthetic was uneventful and the patient's immediate postoperative recovery was rapid and smooth, and she returned to the ward.

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

However, as soon as she was back in bed she started to claw at her neck and to complain that she could not breathe because someone was strangling her. This state cleared within about 2 hours. She appeared neither to have any difficulty with breathing, nor was she ever cyanosed. The nurse repeatedly told her to take deep breaths and she did so without difficulty.

This behaviour might have been due to laryngeal spasm, to oedema, to bronchospasm or to neuromuscular/muscular impairment. However, there was no reduction of air entry either during the anaesthetic or afterwards and, when instructed, she could take a deep breath without difficulty. One possible explanation is an allergic response to propofol or to the vehicle that contains soyabean oil and purified egg phosphatide. It seems unlikely, however, that an allergic response would be delayed until after the patient had recovered consciousness.

Anaesthetics affect the cerebral neurochemistry. Propofol in a susceptible subject may alter the cerebral neurochemistry in such a way as to cause hallucinations. This certainly seems a possible explanation, since the first thing she asked on return to the ward was that a video (non-existent) be turned off. She was also amnesic for the period during which the phenomenon occurred. The content of the hallucination would be difficult to explain unless the patient had some residual recollection of the temporary respiratory depression that followed the injection of propofol and (or) the sensation of the anaesthetist's fingers holding the facemask in position. In a review[1] it was noted that a number of different drugs (propranolol and benzodiazepine withdrawal) and disorders (schizophrenia and sensory deprivation) can, in some people, result in very similar disturbances and hallucinations; there also seems to be a genetic predisposition to hallucinations. It seems, therefore, that a possible explanation for the clinical picture is an unusual alteration of cerebral neurochemistry in a person with a congenital predisposition. This would also explain why the problem arose only after recovery from the anaesthetic.

Whatever the mechanism, the patient has been advised to warn future anaesthetists about the problem.

Princess Margaret Rose Hospital,
Edinburgh EH10 7D
E.L. Lloyd

Reference

1. Lloyd EL. *Hypothermia and cold stress.* London: Croom Helm, 1986: 77–157.

Nerve blocks for hip surgery

We agree with Drs Smith and Allison (*Anaesthesia* 1987; **42**: 296–8) that a nerve stimulator is a very useful aid for the successful performance of sciatic nerve blockade but we have some reservations about the selection of patients for their study.

The nerve supply to the hip joint is derived predominantly from nerves of the lumbar plexus (femoral, obturator and, when present, accessory obturator nerve), although some innervation may arise from the sacral plexus via the nerve to quadratus femoris and superior gluteal nerve.[1–3] However, these nerves leave the sacral plexus above the sciatic foramen and will not be blocked in combination with the sciatic nerve. The area of skin incision and muscle damage for internal fixation is within the distribution of the lateral cutaneous and femoral nerves.

The sciatic nerve sensory component is distributed predominantly below the knee (hence the authors tested for sensory loss in this area) and is not an appropriate block either for surgery or postoperative analgesia for internal fixation of fractured neck of femur. Block of the lateral cutaneous, femoral and obturator nerves, either individually or in combination as either a lumbar plexus block[4] or the so-called 3 in 1 block of Winnie,[5] would have been more appropriate both for surgical and postoperative analgesia.

We question the ethical acceptability of this study, the intention of which was to perform a nerve block of no benefit to the patient in terms of surgical anaesthesia or postoperative analgesia.

St Thomas' Hospital,
London SE1 7EH
A.S.C. Rice
C. Pither

References

1. Williams PL, Roger W. In: *Gray's anatomy*, 36th edn. London: Churchill Livingstone, 1980: 478.
2. Romanes GJ. In: *Cunningham's textbook of anatomy*, 12th edn. Oxford: Oxford University Press, 1981: 246.
3. Gardner E. Innervation of the hip joint. *Anatomical Record* 1948; **101**: 353–71.
4. Chayen D, Nathan H, Chayen M. The psoas compartment block. *Anesthesiology* 1976; **45**: 95–9.
5. Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anaesthesia. The '3 in 1' block. *Anesthesia and Analgesia* 1973; **52**: 989–96.

A reply

We would like to thank Drs Rice and Pither for their comments and *Anaesthesia* for the opportunity to clear up some of the confusion which our original article has produced.

In order to preserve the brevity and clarity of the paper we detailed only the sciatic block. In fact, all patients had several other blocks which are discussed below. Before doing so, however, we would like to discuss some of the other points raised in more detail.

In our experience the nerve to quadratus femoris, posterior cutaneous nerve of the thigh and the gluteal nerves are usually blocked at the same time as the sciatic nerve and, indeed, pudendal block has occurred on more than one occasion. X ray studies using contrast media via a sciatic catheter[1] have shown that retrograde spread of solution occurs along the neurovascular plane of the sciatic nerve somewhat after the manner of the '3 in 1' block, especially if the patient is then positioned with the blocked side uppermost.

The sciatic nerve supplies the hamstring compartment[2] and it is almost invariable that the surgeon trespasses into this area with retractors and other instruments during femoral neck surgery and, indeed, may even pinch the sciatic nerve against the posterior surface of the femur. The sciatic nerve also supplies the ischial fibres of the adductor magnus[2] and failure to block the sciatic nerve leaves significant adductor power which the surgeon may find irritating. The sciatic nerve, via its fine perforating branches, supplies a strip of fascia lata and skin on the posterolateral aspect of the thigh[2], an area into which surgeons again trespass fairly commonly, especially with drains.

We also disagree that the area of skin incision is confined to the lateral cutaneous nerve and femoral nerve distributions, since the skin overlying and above the greater trochanter is supplied by the lateral cutaneous branch of the subcostal nerve (T_{12}).[2] This nerve is most easily blocked by subcutaneous infiltration into the region of the iliac crest.

Therefore, in all our patients the femoral, sciatic, obturator, lateral cutaneous nerve of the thigh and lateral cutaneous branch of T_{12} were blocked. Most femoral neck surgery can be carried out on conscious patients without any discomfort with this combination. Failure to block the sciatic nerve becomes all too readily apparent in such patients both intraoperatively and postoperatively. Conversely, the quality of anaesthesia in most patients would support our view that retrograde spread of the solution does occur.

As a final practical point, hip patients were chosen for the study as the area of testing—the foot—is remote from the operative site and avoids problems of assessment through dressings, plaster of Paris and so on, and is less influenced by patient apprehension than would be the case with surgery to the lower leg or foot.

We feel, therefore, that to study these patients was entirely ethical and, as we pointed out in the paper, all patients, following a detailed explanation of the study, gave formal consent and not just informed consent, as is so often the case.

The Alexandra Hospital,
Redditch B98 7UB

B.E. Smith
A. Allison

References

1. Smith BE, Fischer HBJ, Scott PV. Continuous sciatic nerve block. *Anaesthesia* 1984; **39**: 155–7.
2. Last RJ. *Anatomy—regional and applied*, 5th edn. London: Churchill Livingstone, 1972: 545–50.

Repeated use of halothane

Repeated halothane anaesthesia is no longer a technique that can be endorsed. The usefulness of such a potent agent when faced with heavily built day patients or when an inspection of the larynx prior to neuromuscular block is indicated, is well accepted. Opioid supplements or total intravenous techniques are possible alternatives but the respiratory depression they induce may be particularly hazardous when tracheal intubation is already suspected to be difficult. Enflurane is less potent than halothane and the need for a high inspired concentration may be difficult to achieve with the maximum output of 5% from an Enfluratec. A higher concentration may readily be obtained by the use of two vaporizers in series using both Selectatec mountings as commonly found on anaesthetic machines. Analysis of the outflow using an Engström Emma revealed concentrations never greater than the arithmetic sum of the two concentrations set on the vaporizers. The output was near to the sum of the set concentrations at flows below 5 litres/minute; as the total flow increased the output decreased below the arithmetic sum of the set values on each vaporizer. Analysis has shown concentrations of 9% when both vaporizers are set to 5% with a flow greater than 7 litres/minute. Thus, if an inhalational technique is indicated, a concentration of 9% may be achieved by use of readily available equipment in the department. We would not, of course, recommend this for other than spontaneously breathing patients where the depth of anaesthesia may be gauged clinically.

Whiston Hospital,
Prescot,
Merseyside L35 5DR

R.R. Macmillan
L.J. Colville

A basic problem at cardiac arrests

A recent case serves to re-emphasise the dangers associated with the indiscriminate use of sodium bicarbonate at cardiac arrests.

A 65-year-old Caucasian man was admitted for selective angioplasty of the hepatic artery for treatment of carcinoid metastases in the liver. He suffered a sudden cardiac arrest after 2 weeks in hospital and was promptly resuscitated. He suffered a further arrest 2 hours later and was again resuscitated. This time, however, his trachea was intubated and he was admitted to the intensive care unit. On each occasion he received an infusion of 8.4% sodium bicarbonate from a Polyfusor bottle (Boots Pharmaceuticals); he probably received between 300 and 400 ml in total, although the exact dose was not accurately recorded. On arrival in the ICU his arterial blood gas analysis showed the following: pH 7.42, $P\text{aco}_2$ 10.5 kPa, $P\text{ao}_2$ 6.9 kPa ($F\text{io}_2$ 1.0), standard HCO_3^- 47 mmol/litre, base excess +22.5 mmol/litre. Consequently he was treated with arginine monohydrochloride in a dilute solution to provide an H^+ load of 180 mmol over a 12-hour period. In addition, he was started on acetazolamide (250 mg t.d.s.) and the blood gases and serum electrolytes were checked regularly and corrected appropriately. His acid-base status subsequently returned to normal over the next 36 hours.

The current recommendations of the Resuscitation Council in Great Britain are that in cases of ventricular fibrillation 50 ml 8.4% sodium bicarbonate should be given between the fifth and sixth defibrillation attempts. In other arrest situations bicarbonate should be given only to correct a biochemically proven metabolic acidosis. Bicarbonate may aggravate pre-existing hypokalaemia and the increase in $P\text{aco}_2$ produced by the reaction between HCO_3^- and H^+ may exacerbate cerebral oedema. In addition, an inappropriate bicarbonate infusion can induce both hypernatraemia and a hyperosmolar state. Recently, a retrospective study which followed up patients who were successfully resuscitated following an arrest, demonstrated a poorer outcome when bicarbonate was given than when it was not.[1]

We checked the resuscitation trolleys in our hospital and found that all were stocked with Polyfusor 8.4% bicarbonate infusions (containing 200–300 ml of solution) and 50-ml syringe injection systems (International Medication Systems).

In conclusion, we recommend that infusions of bicarbonate be removed from resuscitation trolleys and be stored separately. This will avoid an infusion being started and subsequently overlooked in the heat of the moment. The use of a single dose injection system containing 50 ml sodium bicarbonate 8.4% gives a safer, more easily recordable quantity of bicarbonate when indicated.

University Hospital of Wales, S.M. Dumont
Cardiff CF4 4XW S. Mousdale

Reference

1. Weil MH, Ruiz CE, Michaels S, Rackow EC. Acid–base determinants of survival after cardiopulmonary resuscitation. *Critical Care Medicine* 1985; **13:** 888–92.

Nomenclature of circle absorption breathing systems

The article by Twigley and her colleagues (*Anaesthesia* 1987; **42:** 419–24) contains a welcome and interesting account of the use of new British equipment which is designed to be used with circle/absorber breathing systems.

The authors refer to it as a 'closed' system whereas, in fact, they used fresh gas flows from two to eight times the flow which can be introduced into a circle system which is closed. The definition of such a system is one 'from which no expired mixture is discharged'.[1] It differs in important respects from the same system into which a flow of 1 litre/minute is introduced. May I make a plea, already made by a previous Editor of *Anaesthesia*[2] and backed by the British Standards Institution,[1] that the terms semi-closed and semi-open are dropped and circle systems are only described as closed when they are truly closed?

Shackleton Department of Anaesthetics, P.J. Horsey
Southampton General Hospital,
Southampton SO9 4XY

References

1. British Standards Institution. *Glossary of terms used in anaesthesiology*. BS 6015 1980. London: British Standards Institution, 1980.
2. Boulton TB. Anaesthetic circuits and systems. (Editorial). *Anaesthesia* 1979; **34:** 605–7.

Editor's note

This error is acknowledged. Our preferred terms *are* breathing system, circle (breathing) system, as appropriate.

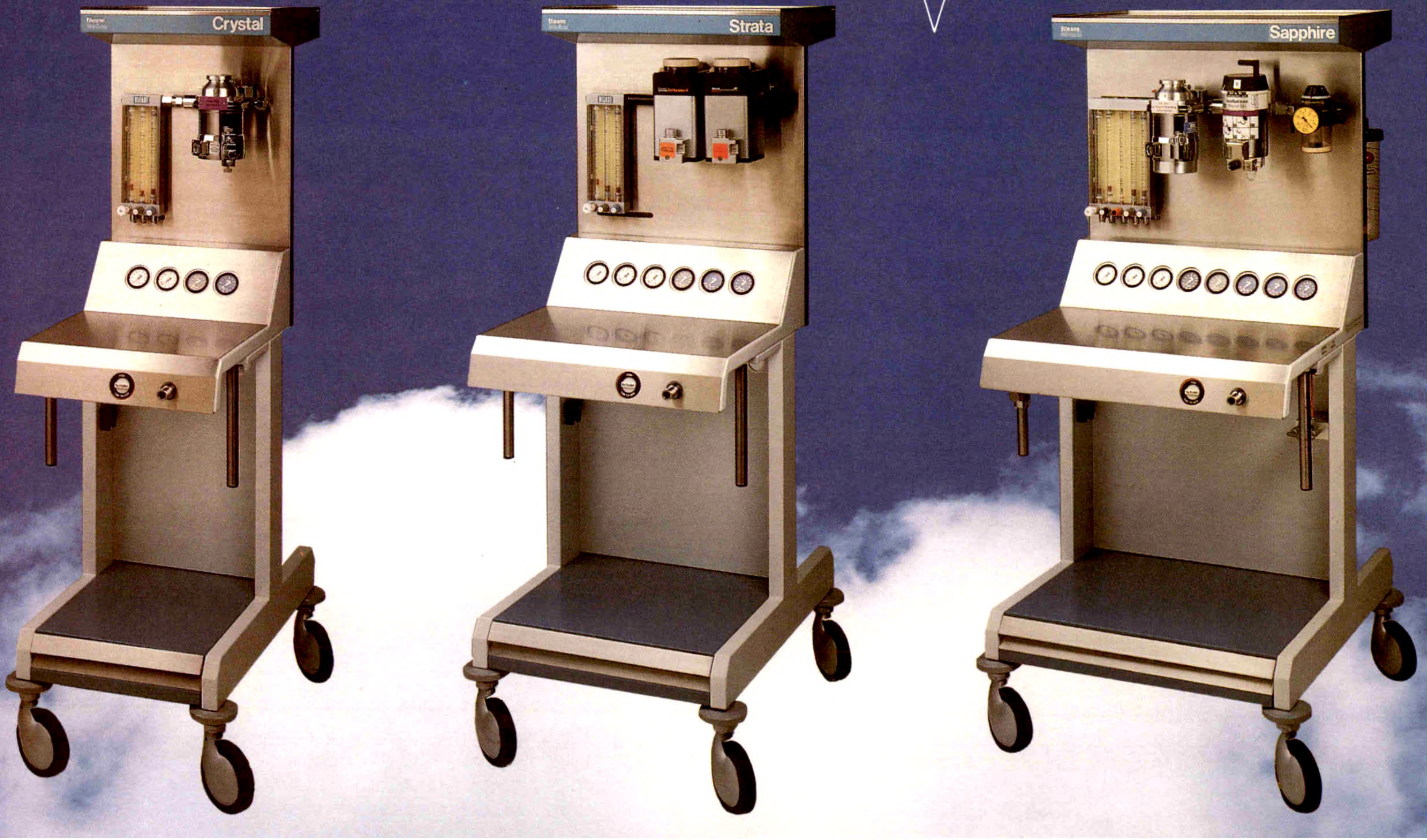
A reply

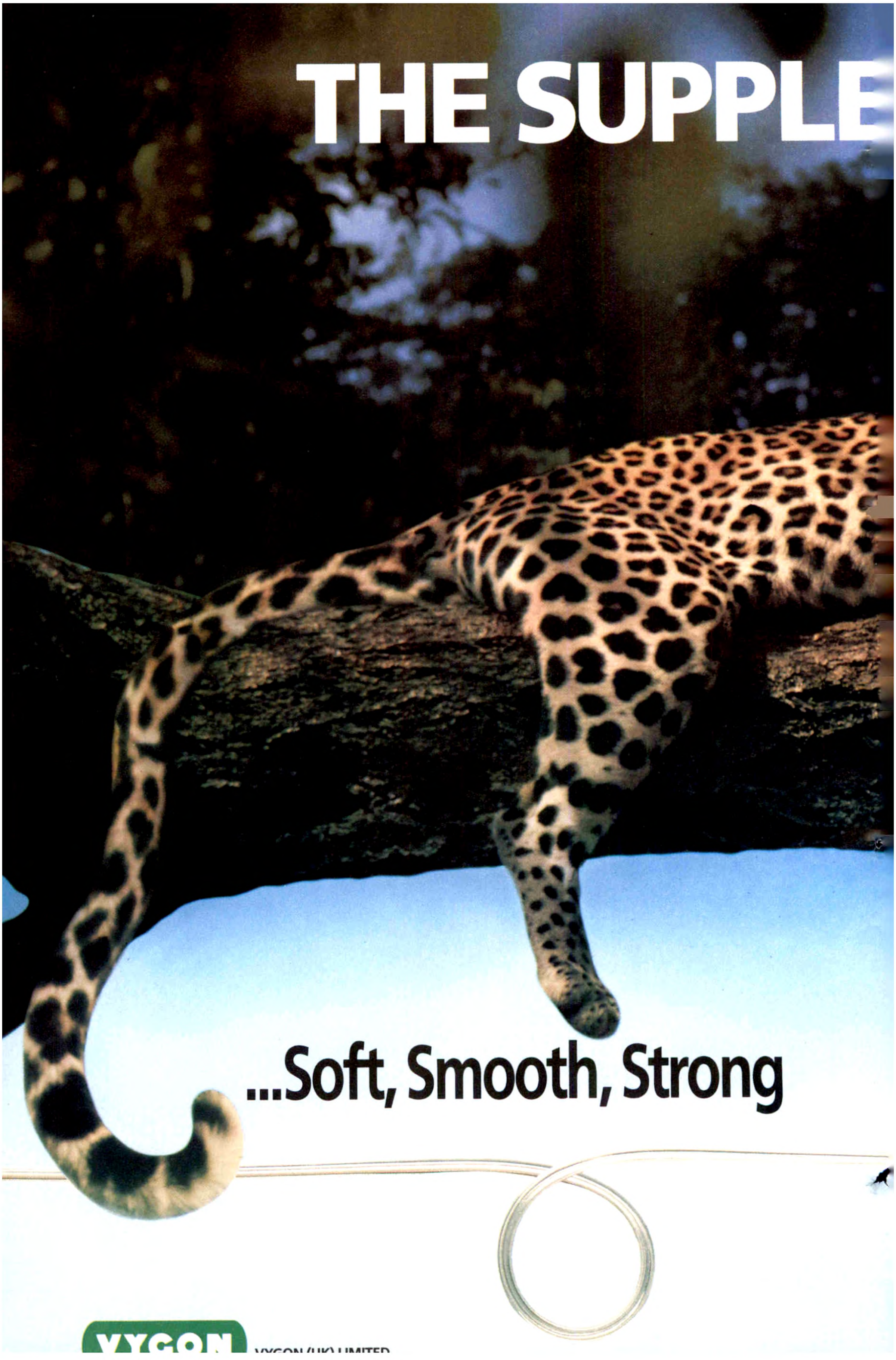
We wish to thank Dr Horsey for drawing our attention to the nomenclature of circle absorption breathing systems. Perhaps we should have used the term 'circle or low flow systems' rather than 'closed', which would imply only basal oxygen input to such a system. The paper speaks for itself but it is reassuring to see that

Blease
Medical

Deansway, Chesham, Bucks HP5 2NX England
Telephone UK: Chesham 784422/3 (STD 0494)
International: 44 494 784422
Telex: 83119 Blease G

ANAESTHETIC
MACHINE RANGE




THE SUPPLE
...Soft, Smooth, Strong
VYGON
VYGON (UK) LIMITED

FLEXANE™

DEVELOPED TO OUTPERFORM ALL OTHER CATHETER MATERIALS

FLEXANE™ IS USED IN THE MANUFACTURE OF MULTICATH TRIPLE AND DOUBLE LUMEN CENTRAL VENOUS CATHETERS

FOR FURTHER DETAILS ON MULTICATH, COMPLETE AND RETURN THIS COUPC

VYGON **VYGON (UK) LIMITED**
BRIDGE ROAD, CIRENCESTER, GLOUCESTERSHIRE GL7 1PT

A1

Name ____________________

Title ____________________

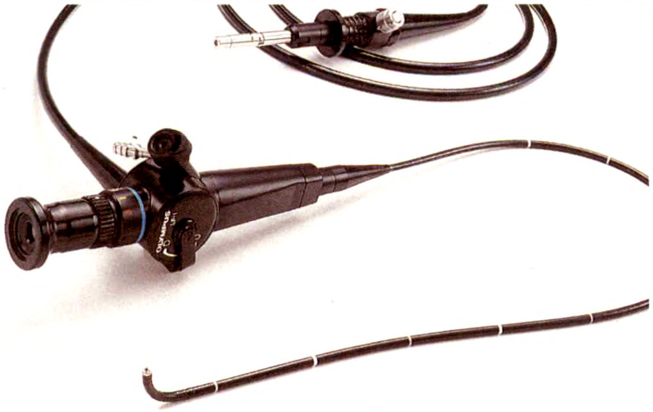
Hospital ____________________

Dept. ____________________

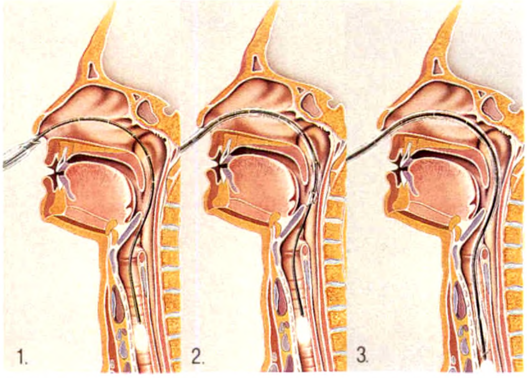
City ____________________

OLYMPUS ENDOSCOPY SYSTEM LF-1 INTUBATING FIBERSCOPE

Specifically designed for anaesthetic use



Fiberoptic bronchoscopes have proved their value for intubating difficult cases*. The LF-1, which is less expensive than current models of bronchoscopes, has been designed to meet the special demands of the procedure. The slimline insertion tube allows a wide range of ET tube diameters to be used, whilst the ergonomic design makes it simple to operate. The LF-1 is an instrument from the OES (Olympus Endoscopy System) range, with the proven benefits of increased durability and immersibility for sterilisation.



1. The LF-1 with the endotracheal tube near the control body, is passed transnasally deep into the trachea.

2. The ET tube is advanced through the nasopharynx using the LF-1 as a 'guide wire'.

3. The ET tube is placed in the trachea, under direct visual control.

---

* 1. Fiberoptic bronchoscopy for anaesthesia. Watson, C.B., Anaesthesiology Review (1982), IX: 17-25.
2. Use of flexible fiberoptic bronchoscope to change endotracheal tubes in critically ill patients. Rosenbaum, S.H., Am. Soc. Anaesthes. (1981), 54: 169-170.
3. Endotracheal intubation with the flexible fiberoptic bronchoscope. Davidson, T.M. Anaesthesiology Review (1975), 54: 346-349.
4. The Broncho-fiberscope as an aid to endotracheal intubation. Taylor, P.A. and Towey R.M. B.J. Anaesth. (1972), 44: 61.

For a demonstration, call Medical Customer Liaison.

OLYMPUS ENDOSCOPY SYSTEM

KeyMed
Specialised Services to Medicine
KeyMed (Medical & Industrial Equipment) Ltd.
KeyMed House, Stock Road, Southend-on-Sea, Essex SS2 5QH.
Telex: 995283, Facsimile: (0702) 65677, Telephone: (0702) 616333 (20 lines).

with subsidiaries:
KeyMed (Ireland) Ltd.
KeyMed House, Lord Edward Court,
Bride Street, Dublin 8.

KeyMed Inc.
400 Airport Executive Park,
Spring Valley, New York, 10977.

someone takes the trouble to ensure the terminological exactitude of the semantics of the art.

However, perhaps we could take this opportunity to add our perceptions to the semantics debate, if only to provoke vigorous discussion. Even when a ventilator can function as a true closed system, in clinical practice it must, for reasons of safety, be provided with a blow-off valve to discharge any excess gas in the breathing system and reservoir bag, and with an entrainment valve to protect against insufficient respiratory gas in the system. Theoretically, only a supply of oxygen and anaesthetic gases equal to the consumption by the patient should be adequate but, clinically, this is a difficult proposition since such oxygen and anaesthetic gas consumption varies all the time during a surgical procedure. Therefore, such practice is potentially unsafe for the patient, for all but the shortest procedures, without a relatively expensive continuous gas monitoring system. Vaporizers may not function accurately at such low flow rates and, for example, the flow rate of nitrous oxide may become very critical. Considering all the circumstances and expense, there seems to be very little benefit in the use of oxygen and anaesthetic gases at a basal flow rate sufficient just to meet patient demand without any blow off of gases from the system. Further, even with a closed system, at the beginning of anaesthesia high flow rates of fresh gases are required to cater for nitrogen washout and to charge the system during the initial rapid phases of the various exponential events which are involved. This requires a discharge of anaesthetic gases from the 'closed' system. Therefore, one wonders whether the rigorous application of the term 'closed system' does not, in practice, prevent this term ever being applicable during clinical practice.

Luton & Dunstable Hospital, A. TWIGLEY
Lewsey Road, Luton, Beds.
Royal Postgraduate M.K. CHAKRABARTI
Medical School, J.G. WHITWAM
Hammersmith Hospital,
Ducane Road, London W12 0HS

A test for breathing systems

Dr Jack (*Anaesthesia* 1987; **42:** 564) stated his drill does not detect the blocked scavenging outlet of a Bain coaxial breathing system. The following test, which we use in this hospital, would have done so and also reduces the frequency of unexpected obstruction of the expiratory valve components. It is a modification of a test recommended in a textbook[1] designed to detect a leak in a breathing system. The advice given is to close the expiratory valve of such systems and, at the same time, to occlude the open patient end and watch the reservoir bag fill with oxygen. The bag is then squeezed so as to test for leaks. If this test is complemented by repetition with the expiratory valve open, a jammed Heidbrink valve (jammed open, bag inflates poorly or, if jammed closed, resistance to bag squeezing) is detected and it would have revealed the problem Dr Jack encountered (resistance to bag squeezing). No test prevents insertion of foreign objects into the system; this one might have assisted in the removal of the offending bottle top!

Royal Hallamshire Hospital, C.M.S. COOPER
Sheffield S10 2RX

Reference

1. WARD CS. *Anaesthetic equipment: physical principles and maintenance*, 2nd edn. London: Baillière Tindall, 1985.

Shelf-life of sodium citrate (0.3M)

There is renewed interest in alternative antacids. The study by Murrell and Rosen (*Anaesthesia* 1986; **41:** 138–42) into Alka Seltzer effervescent correctly points out some limitations in magnesium trisilicate mixture and sodium citrate (0.3M). However, we take issue on the statement that 'Sodium citrate (0.3M) only has a shelf-life of about 8 weeks'.

This statement seems to result from a misinterpretation of another study[1] which examined glass vials of sodium citrate (0.3M) either at room temperature or refrigerated to 4°C. The experiment was continued for 8 weeks only, at which stage no significant change of pH had occurred. Similarly, another group[2] concluded that the solution 'remains stable for at least 2 months'. Both of these studies examined sodium citrate (0.3M) solution for approximately 2 months but, apparently, not beyond this time.

A clinical study[3] of sodium citrate (0.3M) demonstrated that the preparation maintained its pH at 8.5 for 12 months. The solution was also shown to maintain its clinical efficacy over this period. Other potential problems listed by Murrell and Rosen such as 'interaction with the atmosphere, crystallising of the syrup or interaction with silica in the glass of the container', did not appear to occur.

Currently, at this hospital the sodium citrate (0.3M) solution is produced by our pharmacy using the method described by Lahiri *et al.*[2] It is stored in sealed clear glass containers and given an expiry date of one year from manufacture. We believe that storage for this period of time does not interfere significantly with the clinical safety or efficacy of sodium citrate (0.3M) solution.

The Queen Victoria Hospital,
Adelaide, Australia

R. BURGESS
J. WROBEL

References

1. ABOULEISH E, SCHENLE IA. Efficacy of antacid therapy. *British Journal of Anaesthesia* 1977; **49**: 394.
2. LAHIRI SK, THOMAS TA, HODGSON RMH. Single-dose antacid therapy for the prevention of Mendelson's syndrome. *British Journal of Anaesthesia* 1973; **45**: 1143–6.
3. WROBEL J, KOH TC, SAUNDERS JM. Sodium citrate: an alternative antacid for prophylaxis against aspiration pneumonitis. *Anaesthesia and Intensive Care* 1982; **10**: 116–9.

Prolonged neuromuscular blockade in an infant

We would like to report a case of prolonged neuromuscular blockade that occurred in an infant.

A 2-month-old infant with acyanotic congenital heart disease presented with failure to thrive. She subsequently developed respiratory distress and required ventilation of her lungs for 7 days. Neuromuscular blockade was achieved with a vecuronium infusion at a rate of 1.67 μg/kg/minute. This was reduced to 0.83 μg/kg/minute after 5 days. She made no respiratory efforts 24 hours after the infusion was stopped and no twitch of adductor pollicis was detectable on train-of-four (TOF) stimulation of her ulnar nerve. Neostigmine and atropine produced a marked improvement in the TOF response and the infant commenced respiratory and voluntary movements. She redeveloped a neuromuscular blockade over a period of 2 hours and again required ventilation. Vecuronium levels measured in the blood 24 hours after the infusion was stopped (0.31 μg/ml) were consistent with 95% twitch depression.[1] The infant regained full neuromuscular function over the next 48 hours.

The administration of neuromuscular blocking agents to infants who need prolonged ventilation with acquired respiratory pathology or congenital heart disease is an established technique.[2] The lack of accumulation, ease of reversal and cardiovascular stability of vecuronium make it an attractive agent for this purpose. We were surprised to find a profound neuromuscular blockade 24 hours after vecuronium was stopped and that its reversal with neostigmine was temporary.

Previously two infants who received similar long-term ventilation had persistent neuromuscular blockade after withdrawal of vecuronium. Both infants had several potentially complicating factors: renal abnormality, concurrent aminoglycoside administration, serum potassium irregularities and hydrogen ion imbalances. The case we report had none of these complicating factors. In each of these other cases recurarisation occurred over a 2-hour period following neostigmine and atropine. Subsequent analysis of blood samples demonstrated vacuronium levels consistent with 95% twitch depression which persisted, in one case, up to 9 days following its withdrawal.

The dose of vecuronium in infants has yet to be established. Fisher *et al.*[3] used a vecuronium infusion of 2.5 μg/kg/minute to determine vecuronium kinetics in infants and children but the duration of the infusion was probably less than 10 minutes. Infusion rates of 1.4 μg/kg/minute for up to 5 hours have been used in adults.[4] This case demonstrates that significant accumulation occurs in infants.

In retrospect, our initial use of 1.67 μg/kg/minute of vecuronium, decreasing to 0.83 μg/kg/minute, was excessive. The production of a profound, prolonged neuromuscular blockade in this infant following long-term administration of vecuronium might have been avoided if monitoring of the neuromuscular junction had been undertaken.

We thank John Hamilton of the Biochemistry Department, Yorkhill for help in preparation of the samples and W.P.T. Chitty of Organon Technica for arranging the measurement of the vecuronium levels.

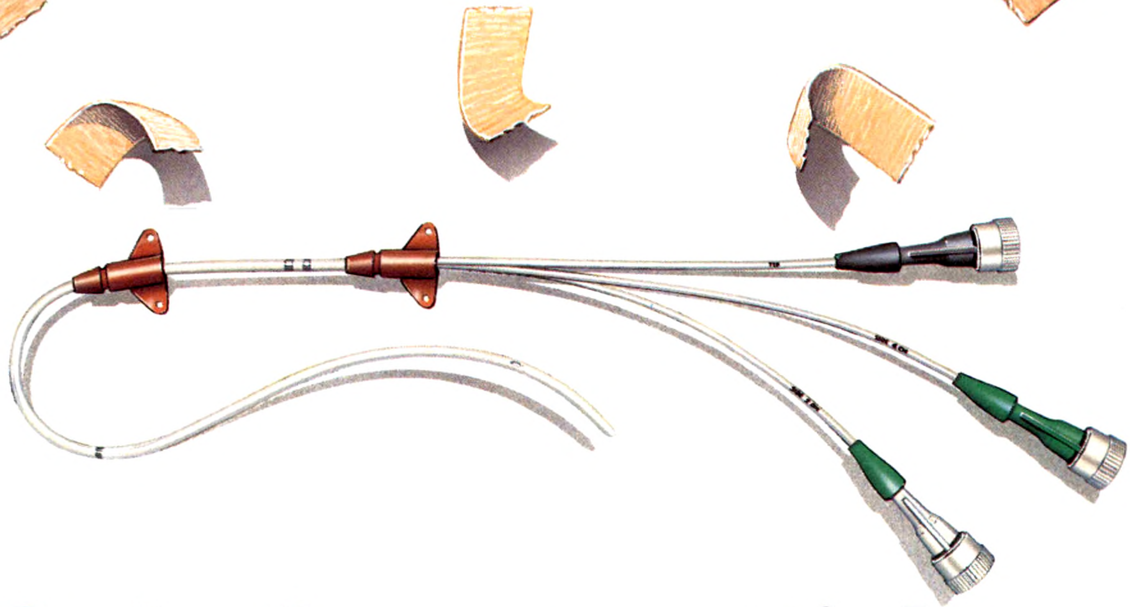
Royal Hospital for Sick Children,
Glasgow G3 8SJ

J.F. SINCLAIR
G.A. MALCOLM
J.B.P. STEPHENSON
D. HALWORTH

References

1. SHANKS CA. Pharmacokinetics of the nondepolarizing neuromuscular relaxants applied to calculation of bolus and infusion dosage regimes. *Anesthesiology* 1986; **64**: 72–86.
2. GREGORY GA. Respiratory failure in the child. In: *Clinics in critical care medicine, Vol. 3.* Edinburgh: Churchill Livingstone, 1981: 25.
3. FISHER DM, CASTAGNOLI K, MILLER RD. Vecuronium kinetics and dynamics in anaesthetized infants and children. *Clinical Pharmacology and Therapeutics* 1985; **37**: 402–6.
4. MIRAKHUR RK, FERRES CJ, PANDIT SK. Muscle relaxation with an infusion of vecuronium. *Anesthesiology* 1984; **61**: A293.

Hydrocath®



Only the name sticks.

HYDROMER® is the special hydrophilic polymer that protects all HYDROCATH® catheters. When activated by body fluids it creates an aqueous complex which surrounds the catheter.

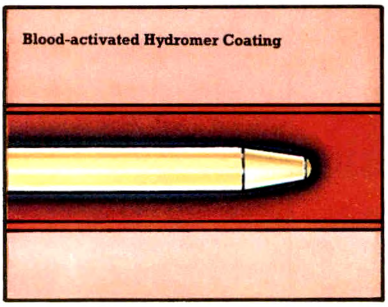
This complex reduces the surface friction of the catheter to less than that of wet glass, making insertion easier and reducing patient trauma.

Once in situ the Hydromer coat remains activated, creating a barrier at the blood/catheter interface.

For more information on the complete range of Secalon® Hydrocath central venous catheters please telephone (0793) 641791 or write to "Hydrocath", Viggo, P.O. Box 77, Swindon, Wiltshire, U.K.

® = Registered Trademark

SEE HYDROCATH ON THE VIGGO STAND AT THE ASSOCIATION OF ANAESTHETISTS MEETING IN SHEFFIELD



Viggo

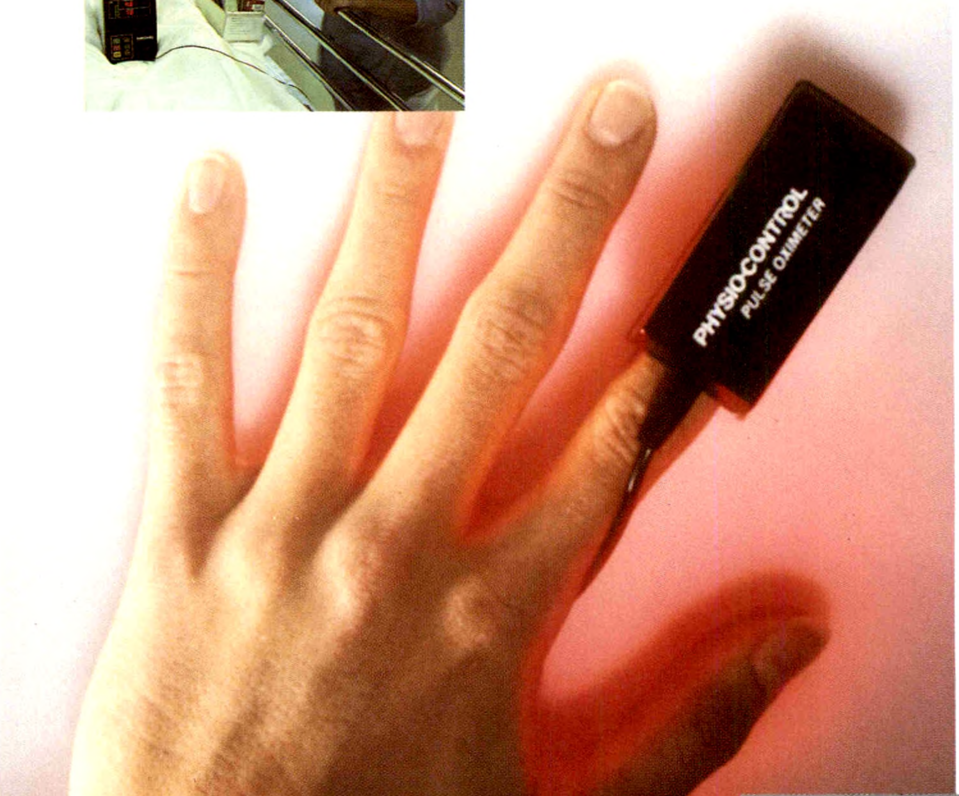
British Viggo
Faraday Road
Swindon
Wiltshire SN3 5HZ
Tel: 0793 641791
Telex: 444443 VIGGO G

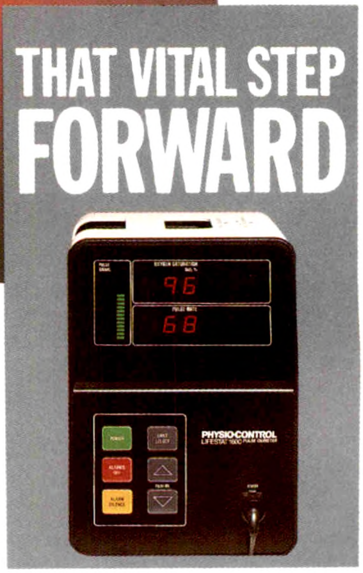
BOC Health Care

Viggo International Sales
Chertsey Road
Windlesham
Surrey GU20 6HJ
Tel: 0276 77222
Telex: 859363 BOC GHQ G
Fax Nos: 0276 71333/77550

PHYSIO CONTROL

Physio-Control Ltd., Intec 2, Units 10-20,
Wade Road, Basingstoke RG24 0NE.
Tel: (0256) 474455 Telex: 858931 ELI EAG
Fax: (0256) 463770
A Lilly Medical Instrument Systems Company.





OUR GOAL: To take Pulse Oximetry that vital step beyond the known parameters.

OUR ANSWER: No ordinary oximeter, but one that combines continuous non-invasive monitoring with exacting new features.

Features such as a temperature compensated sensor that provides truly accurate results and a unique trend indicator to warn you of any short or long term changes. All this in an up-to-the-minute design with easy to view and read displays.

THE LIFESTAT® 1600 PULSE OXIMETER.
It's the one you've been waiting for.

Physio-Control and LIFESTAT are trademarks of Physio-Control Corporation. © 1987 Physio-Control Corporation.

Priming with vecuronium in obstetrics

The priming technique for rapid sequence induction with vecuronium is used safely in nonpregnant patients. We describe two instances where this technique was associated with respiratory depression due to muscle weakness that required immediate tracheal intubation.

The first patient was a 28-year-old white female who weighed 73 kg; she was scheduled for Caesarean section. Vecuronium 1 mg (13.7 μg/kg) was administered intravenously as a priming dose after preoxygenation for 5 minutes. Two minutes later the patient developed difficulty in breathing. The tidal volume decreased from 800 to 200 ml and she could neither open her eyes nor protrude her tongue. She became intensely restless, moved her extremities violently and was unable to breathe. The priming technique was abandoned and rapid sequence induction with thiamylobarbitone and suxamethonium was performed. The baby was delivered safely and had Apgar scores of 8 and 9, respectively, at 1 and 5 minutes after delivery.

The second patient was a 27-year-old white female also scheduled for Caesarean section. In this instance vecuronium 10 μg/kg was administered intravenously as a priming dose. Four minutes after administration of vecuronium, while preparing to inject thiamylobarbitone and the intubating dose of vecuronium, the patient complained of difficulty in breathing and then vomited. Her mouth and pharynx were immediately cleared with suction and the trachea was intubated expeditiously after thiamylobarbitone and suxamethonium. The baby was delivered with Apgar scores of 8 and 10 at 1 and 5 minutes after delivery.

Both patients demonstrated respiratory distress after a priming dose of vecuronium that is considered acceptable in nonobstetric patients.[1,2] Neither patient was on any medication (magnesium sulphate, diuretics or antibiotics) which could possibly potentiate the muscle relaxation produced by nondepolarising muscle relaxants. These two cases illustrate the sensitivity of parturients to small doses of vecuronium (10–15 μg/kg) which are considered acceptable and safe in the nonpregnant population. It would be reasonable to avoid the use of the priming technique in these cases or to reduce the muscle relaxant dose significantly in order to avoid this complication.

Maimonides Hospital,
Brooklyn,
New York 11219, USA

S. Cherala
D. Eddie
M. Halpern
K. Shevde

References

1. Foldes F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs: the priming principle. *British Journal of Anaesthesia* 1984; **56**: 663.
2. Taboada JA, Rupp SM, Miller RD. Refining the priming principle for vecuronium during rapid sequence induction of anesthesia. *Anesthesiology* 1986; **64**: 243–7.

Pain-free intravenous injections

The following technique is helpful in the reduction of pain caused by injection of propofol or methohexitone solution into peripheral veins.

A suitable vein in the dorsum of the hand is cannulated. An assistant then grips the upper arm at mid-biceps level to occlude the veins. One millilitre 1% lignocaine is then injected through the cannula and the venous occlusion is maintained for the next 15 seconds (approximately). The injection of propofol or methohexitone is made and is usually pain free.

There have not yet been complications. There is some increased inconvenience in the preparation of a separate injection of lignocaine but, on the other hand, there is no need to mix drugs in the same syringe.

Princess Margaret Hospital,
Swindon SN1 4JU

R. Porteous

Unexpected difficult intubation

The case reports by Drs Mason and Wark (*Anaesthesia* 1987; **42**: 407–10) were interesting because I had a similar experience a few years ago. A healthy adult was anaesthetised for elective cholecystectomy using thiopentone and pancuronium. There was no difficulty with manual ventilation using a mask and airway but, at laryngoscopy, I was surprised to see a large vallecular cyst that completely obscured the view of the vocal cords. Fortunately, using a bougie and estimating the position of the laryngeal inlet, a blind oral tracheal intubation was possible. The remainder of the anesthaetic and surgery were uneventful. The cyst was aspirated at a later date by an ENT surgeon in outpatients.

Many anaesthetists prefer not to use suxamethonium in intubation for elective surgery so as to avoid its side effects. If they choose to use non-depolarising neuromuscular blockade they should be aware of this rare problem of intubation and of how to deal with it. The ENT surgeon involved in this case suggested that the anaesthetist could aspirate the cyst if that seemed to be necessary.

The General Hospital,
Burton on Trent,
Staffs. DE14 3QH

S.W. Millar

Kinked pilot tube

Dr Mehta (*Anaesthesia* 1987; **42:** 443) appears to have misunderstood our earlier letter (*Anaesthesia* 1986; **41:** 1060). We never intended to suggest that a pilot tube could be compressed within the wall of the tracheal tube. Rather, it was kinked by the retaining bandage just as it left the wall of the tube at its high take-off point. Unfortunately, shortage of space demanded that the original letter be curtailed and the explanatory photograph omitted. The problems Dr Mehta mentions occurred with a different tube (the Mallinckrodt Hi-Lo as opposed to our Mallinckrodt Lo-Pro) and, while interesting, are not related.

The Leicester Royal Infirmary,
Leicester LE1 5WW

J. Tanski
R.H. James

Early textbooks on anaesthesia

A list of 25 books printed in 1847, and about the inhalation of ether (*Anaesthesia* 1985; **40:** 385–6), was published earlier but that list was unlikely to be complete.

Since then I have been looking for more books from 1847. Here is a list of 13 more books and most likely the list, now 38 books, is still not complete. This list adds books from Austria, Czechoslovakia, Switzerland and Hungary. The third book* was mentioned to me by Dr R.K. Calverley, San Diego, California, and should be in the Wood Library Museum. Interestingly enough the foreword is dated 17 February, so it could be earlier than J. Robinson's *A Treatise on the Inhalation of the Vapour of Ether*. Brookes is mentioned in Robinson's book.

Dr R.H. Ellis remarked correctly about the former list that not all the titles are books in the proper sense; those marked with a dagger (†) are written for lay people (incidentally, the writer has seen none of the books).

The main source of this book list is: Walser HH. Zur Einführung der Äthernarkose im deutschen Sprachgebiet im Jahre 1847. *Veröffentlichungen der Schweizerischen Gesellschaft für Geschichte der Medizin und der Naturwissenschaften* 1957; **21:** 1–55.

University Hospital,
DK-2100 Copenhagen,
Denmark

O. Secher

Book list

† Bergson J. *Die medicinische Anwendung der Ätherdämpfe.* Berlin, 1847.

Bibra Ev, Harless E. *Die Wirkungen des Schwefeläthers in chemischer und physiologischer Beziehung*. Erlangen, 1847.

* Brookes, W Philpot. *Practical remarks of the inhalation of the vapour of sulfuric ether illustrated with cases and the latest method of application with remarks as to the proper period to commence operation, &c.* Princess St, Soho, London: John Churchill, 1847.

Gnenser WL. *Über Äther-Einathmungen während der Geburt.* Leipzig, 1847.

Hammer A. *Die Anwendung des Schwefeläthers im Allgemeinen und insbesondere bei Geburten.* Mannheim, 1847.

Jablonski CF. Abhandlung über die Wirkungen der Schwefelätherdämpfe. Dissertation, Bern (Switzerland), 1847.

Jenny JJ. *Erfahrungen über die Wirkungen der eingeahlmeten Schwefelätherdämpfe.* Zurich, 1847.

† Kopezky B. *Warnungen von den schädlichen Wirkungen der Aether-Einathmung.* Wien, 1847.

† Kronser VN. *Der Schwefel-Äther.* Wien, 1847.

Rosenfeld J. *Die Schwefeläther-Dämpfe und ihre Wirksamkeit, vorzüglich in Bezug auf operative Chirurgie.* Pest (Hungary), 1847.

† Schleisinger J. *Die Einathmung der Schwefel-Äthers in ihren Wirkungen auf Menschen und Thiere, besonders als Mittel bei chirurgischen Operationen den Schmerz zu umgehen.* Leipzig, 1847.

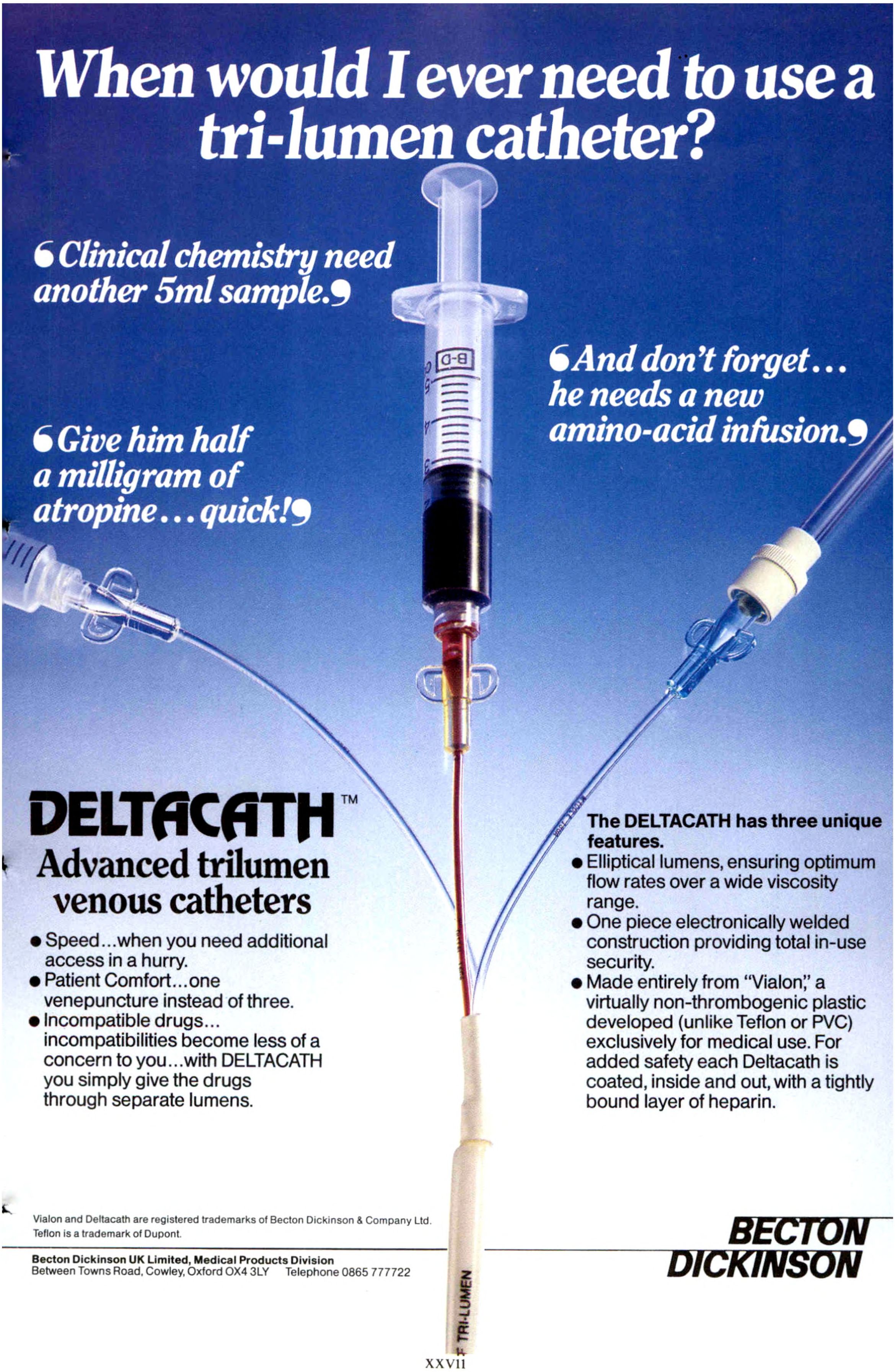
Siebold ECJv. *Über die Anwendung der Schwefeläther-Dämpfe in der Geburtshilfe.* Göttingen, 1847.

† Welz Rv. *Die Einathmung der Äther-Dämpfe in ihrer verschiedenen Wirkungsweise.* Würzburg, 1847.

Beta blockade and nitroprusside

The article on acute beta-adrenoreceptor blockade and induced hypotension by Drs Simpson, Macrae *et al.* (*Anaesthesia* 1987; **42:** 243–8) was interesting. It is common practice in this hospital to induce hypotension with sodium nitroprusside infusions, for surgery of the lumbosacral spine.

Recently, oral labetalol (100 mg) was included with the premedication given 2 hours prior to surgery. A



When would I ever need to use a tri-lumen catheter?

‘Clinical chemistry need another 5ml sample.’

‘And don't forget… he needs a new amino-acid infusion.’

‘Give him half a milligram of atropine… quick!’

DELTACATH™

Advanced trilumen venous catheters

- Speed…when you need additional access in a hurry.
- Patient Comfort…one venepuncture instead of three.
- Incompatible drugs… incompatibilities become less of a concern to you…with DELTACATH you simply give the drugs through separate lumens.

The DELTACATH has three unique features.

- Elliptical lumens, ensuring optimum flow rates over a wide viscosity range.
- One piece electronically welded construction providing total in-use security.
- Made entirely from "Vialon," a virtually non-thrombogenic plastic developed (unlike Teflon or PVC) exclusively for medical use. For added safety each Deltacath is coated, inside and out, with a tightly bound layer of heparin.

Vialon and Deltacath are registered trademarks of Becton Dickinson & Company Ltd.
Teflon is a trademark of Dupont.

Becton Dickinson UK Limited, Medical Products Division
Between Towns Road, Cowley, Oxford OX4 3LY Telephone 0865 777722

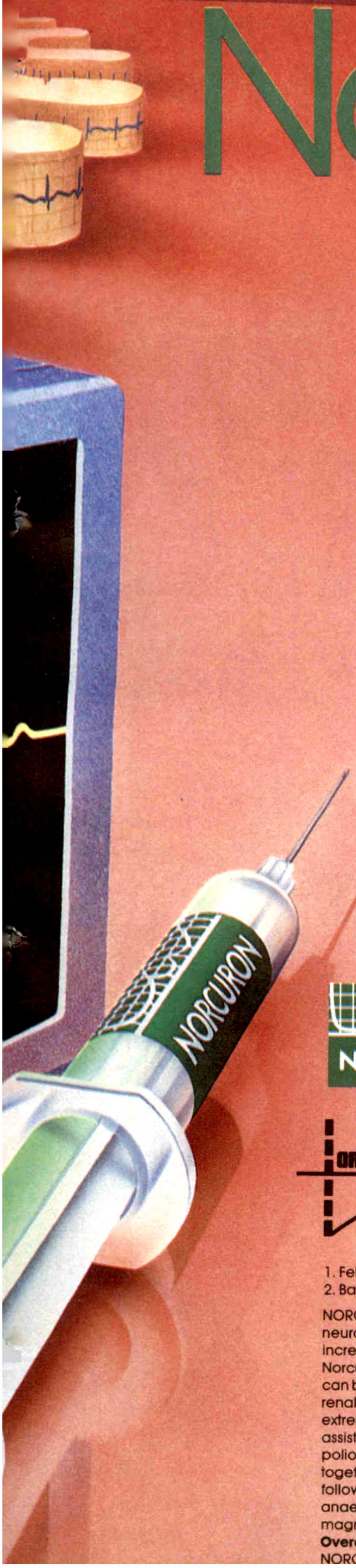
BECTON DICKINSON

Leave behind
muscle relaxant
complications

Muscle relaxation, pure and simple

NORCURON®

vecuronium bromide



Highly specific

Muscle relaxants are known to cause cardiovascular side effects when their action is not specific for the neuromuscular junction.

NORCURON

"...is the most specific neuromuscular blocking agent that has ever been synthesized. It is the drug which has by far the fewest side effects of any neuromuscular blocker. As a result, it has the highest therapeutic ratio".[1]

NORCURON

"Because it is so 'pure', because it is so free from side effects, it can be given in high doses. It can be given at 6, 8, 10 or 15 times the ED_{90} dose, if the clinician so wishes".[1]

Histamine release unlikely

Some muscle relaxants cause histamine release. This may give rise to such side effects as hypotension and bronchospasm.

NORCURON

"...at 3.5 times the ED_{95} does not alter serum histamine levels".[2]

NORCURON

Muscle relaxation, pure and simple.

ORGANON TEKNIKA

Organon Teknika Limited

Cambridge Science Park, Milton Road,
Cambridge CB4 4BH

1. Feldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
2. Basta SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 183-184

NORCURON ampoules of 4mg vecuronium bromide with 1ml ampoule water for injection. **Uses:** non-depolarising neuromuscular blocking agent of short to medium duration. **Dosage:** intravenous initial 0.08 to 0.10mg/kg incremental 0.03 to 0.05mg/kg. **Contra-indications:** none known. Since there is no experience with the use of Norcuron in pregnant women, it cannot be recommended during pregnancy. Clinical studies show that Norcuron can be used in childbirth by Caesarian section without effect on the newly born child. **Precautions and warnings:** in renal insufficiency a slight prolongation of neuromuscular block can be expected. Use very small doses, and extreme caution in myasthenia gravis or myasthenic syndrome unless prolonged post-operative respiratory assistance is intended. Dose carefully in myopathy, severe obesity, electrolyte disturbances, altered pH and after poliomyelitis or dehydration. Neuromuscular blockade can be reversed with adequate doses of neostigmine together with atropine. **Interactions:** it is dangerous to give depolarising drugs (e.g. suxamethonium chloride) following a non-depolarising drug (e.g. Norcuron). Alkylating drugs (nitrogen mustards) may be a hazard in anaesthesia involving muscle relaxants. Anaesthetics, other drugs and the condition of the patient, may affect the magnitude and or duration of action of NORCURON – see Data Sheet. **Side-effects:** none during clinical testing. **Overdosage:** use standard reversal agents. e.g. neostigmine or pyridostigmine. **Packs:** 50 ampoules 4mg NORCURON. 50 ampoules 1ml solvent. **PL:** 3524/0009

VAPAMASTA 5 mie

THE NEW GENERATION OF VAPORIZERS

What do you want from your vaporizer?

- Reliability?
- Ease of service?
- Good value?

MIE can offer all three and more besides.....

SEE US AT THE ASSOCIATION OF ANAESTHETISTS MEETING, SHEFFIELD, SEPT. 9th - 11th, STAND 54.

M.&I.E.
Dentsply

Sowton Industrial Estate, Exeter EX2 7NA. Tel: Exeter (0392) 31331. Telex 42743 Mediex G. FAX (0392) 39927

significant decrease in the total dose of sodium nitroprusside required to maintain mean arterial blood pressure between 60 and 65 mmHg, has been obtained with this regimen.

However, in approximately 20 patients, there was no instance of bradycardia (heart rate less than 50 beats/minute); perhaps this is due to labetalol, which has alpha- as well as beta-receptor blocking activity and therefore is less likely to induce bradycardia. This technique, with reduction in dosage of sodium nitroprusside, is useful.

Nottingham City Hospital,
Nottingham NG5 1PB
N.R. Coad

A reply

Thank you for the opportunity to reply. The apparent absence of bradycardia in these patients pretreated with labetalol may indeed be a consequence of its blocking action on alpha and beta receptors, whereas metoprolol and oxprenolol act on beta receptors alone. However, as we discussed in our paper, the incidence of bradycardia may also be affected by the choice of premedicant drugs, the techniques of induction and maintenance of anaesthesia and the patient population which is studied.

Dr Coad states in his letter that the total dose of sodium nitroprusside required to achieve a mean arterial pressure of 60–65 mmHg was significantly reduced after pretreatment with labetalol. This agrees with our findings in our patients who received metoprolol 50 mg or oxprenolol 20 mg pre-operatively.

It would be interesting to know whether pretreatment with labetalol was associated with any significant improvement in operating conditions or reduction in blood loss.

Royal Hospital for Sick Children,
Edinburgh EH9 1LF
D.L. Simpson

Epidural lavage for extensive epidural suppuration

A 2.5-year-old boy developed extensive epidural suppuration as a complication of an infected haematoma after trauma in the sacral region. There was a congenital dermal sinus which was responsible for the infection.

Creamy pus was obtained from multiple close punctures of the epidural space using Mancao needles[1] from between the sacral hiatus to the mid-thoracic area. The lowest and highest needles were left in place so that lavage with 400 ml normal saline could be carried out over a period of 30 minutes. Lavage was continued until the liquid that emerged was clear. The child was under general anaesthesia with ketamine for this procedure and a multihole catheter was advanced towards the head from the sacral hiatus and, by chance, it reached T_7–T_8. Normal saline 5 ml with gentamicin 2.5 mg was administered every 12 hours. The child improved clinically and neurologically over the following 5 days, after which the catheter was removed. The child is healthy and free of neurological sequelae 18 months later.

There is no doubt that drainage of the abscess played a significant role in the child's improvement and the use of the epidural catheter at such a high level was also beneficial. Neurosurgical text books suggest several kinds of laminectomy as the only therapeutic choice. However, this method should be considered as a suitable alternative in order to avoid extensive or multiple laminectomies in such small patients.[2] This case illustrates the use of the Mancao needle which is designed to avoid accidental dural puncture.

University Hospital,
Cluj Napoca,
Romania
E. Cardan
M. Nanulescu

References

1. Mancao F, Poremski V, Hempel V. Die Mancao-Kanüle—ein neues System zur Erleichterung der Periduralpunktion. (The Mancao cannula—a new system for the facilitation of peridural puncture.) *Regional Anaesthesia* 1983; **6**: 88–90.
2. Fischer EG, Greene CS, Winston KR. Spinal epidural abscess in children. *Neurosurgery* 1981; **9**: 257–60.

Postoperative complications of dystrophia myotonica

Drs Moore and Moore (*Anaesthesia* 1987; **42**: 529–33) state that, 'we could find no reports specifically of the complications that may result from anaesthesia in patients with undiagnosed dystrophia myotonica.' In fact, such a report was published by Dr Bourke and myself[1] and was cited by Dr Kaufman.[2] Our patient also developed pulmonary oedema in the early postoperative period without any obvious reason. Certain of the cases mentioned by Kaufman appear to have succumbed to this complication; for example, 'Bronchial secretions became exceedingly profuse and death occurred eight hours postoperatively.'

It seems that pulmonary oedema, perhaps related to the cell membrane defect, should be recognised as a specific hazard of anaesthesia in dystrophia myotonica, although why the same patient should develop it on one occasion and not on another, remains a puzzle.

Chase Farm Hospital,
Enfield EN2 8JL
D. Zuck

References

1. Bourke TD, Zuck D. Thiopentone in dystrophia myotonica. *British Journal of Anaesthesia* 1957; **29**: 35–8.
2. Kaufman L. Anaesthesia in dystrophia myotonica. A review of the hazards of anaesthesia. *Proceedings of the Royal Society of Medicine* 1960; **53**: 183–8.

A reply

We apologise to Dr Zuck for not spotting his paper. A cell membrane defect might, in theory, account for our patient's postoperative pulmonary oedema but it seems more likely to us that his cardiac disease was responsible. The main purpose of our article was to illustrate the diverse postoperative problems associated with myotonic dystrophy. If such problems occur unexpectedly then dystrophia myotonica should be considered as an underlying diagnosis.

Royal Infirmary,
Glasgow G31 2ER
J.K. Moore
A.P. Moore

Early retirement and morbidity

The attempt by Dr McNamee and colleagues (*Anaesthesia* 1987; **42:** 133–40) to relate morbidity to early retirement is ingenious but I suggest that the conclusions they draw from their data are unwarranted. That 65 years of age is the normal age for retirement is true only insofar as 65 is the statutory age, but it does not make it abnormal to retire earlier. Most people retire when they choose to do so, for a wide variety of reasons. I submit that the fact that someone has resigned from an NHS appointment at a certain age, tells you no more than just that fact. It does not mean that they have retired from anaesthetic or any other sort of active practice and to suggest that it implies some vague sort of ill health, is unjustifiable.

It would be surprising if employing authorities had any real knowledge about why consultants resign before they attain 65 years of age, and I applaud those authorities who refused to give information about consultants' state of health for reasons of confidentiality.

The authors suggest that a possible cause of stress and lack of job satisfaction may be that anaesthetists have less sustained contact with patients than others. They seem unaware that some people take up anaesthetics for precisely this reason. Short periods of intense responsibility are much more satisfying for many people than the long-term care of chronically ill patients.

The authors rightly criticise previous studies of morbidity as unsatisfactory but it seems to me that theirs is even more lacking in objectivity than most.

90 High Street,
Great Abington,
Cambridge CB1 6AE
A.K. Adams

The interest of McNamee, Keen and Corkell in the mortality and morbidity of our colleagues seems to me to be somewhat macabre (*Anaesthesia* 1987; **42:** 133–40). I would rather have heard of the interesting things that are done by those who have taken early retirement while quite fit. In this context if any 'early retirers' feel like extending their anaesthetic career why not consider working for the University of Zimbabwe for a year or two? Anaesthesia here is endlessly fascinating and the climate, near perfect. The salary is adequate.

Harare Central Hospital,
Box St 14,
Southerton,
Harare, Zimbabwe
R. Hutchinson

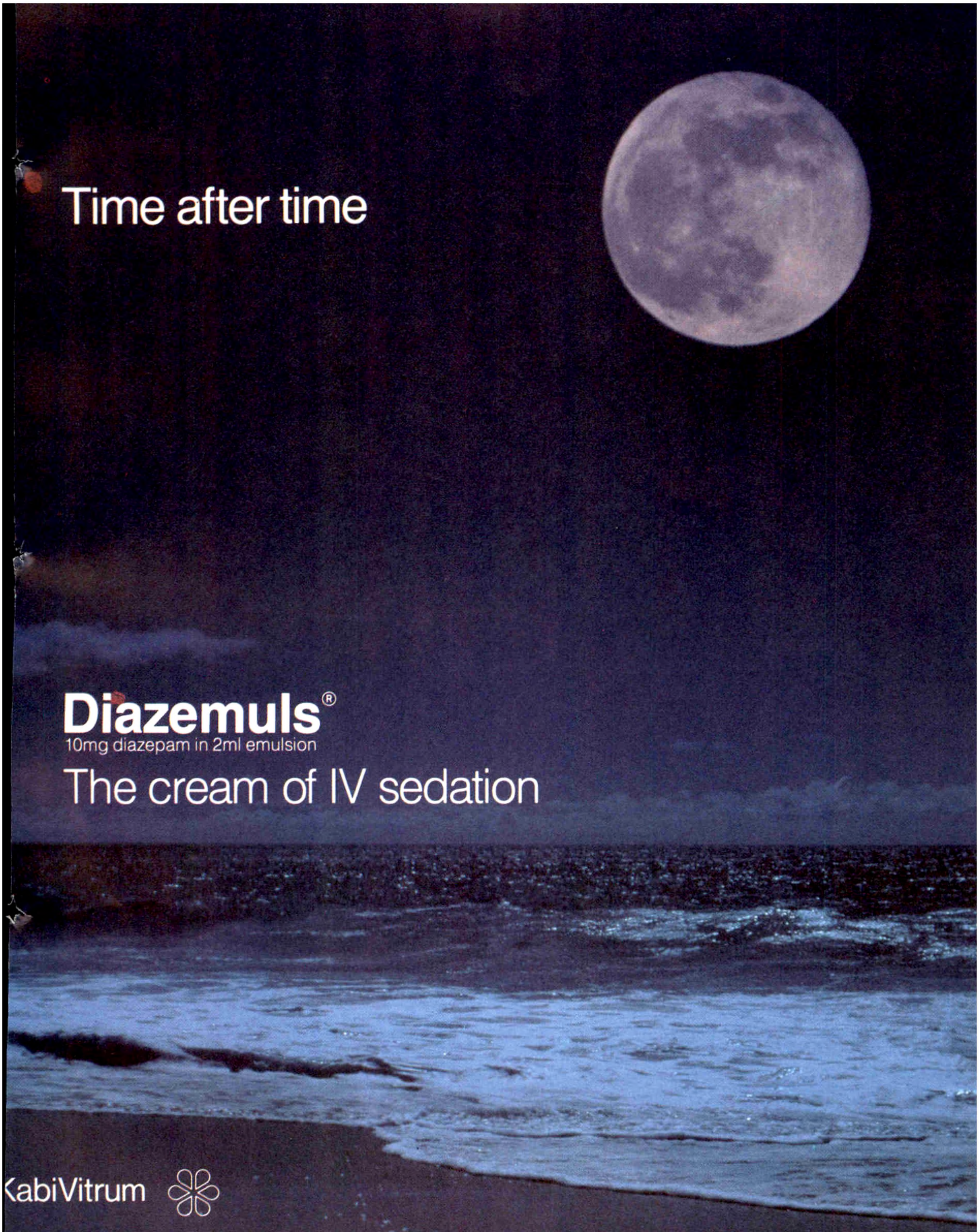
A reply

Thank you for allowing us to see Dr A. K. Adams' letter about our paper (*Anaesthesia* 1987; **42:** 133–40). We regret her comments but stand by our findings. Some clarification might be helpful. The retirements on which the main comparisons were based, were due to permanent ill-health as reported to us by employing authorities. These would certainly not accept Dr Adams' 'some vague sort of ill health' as a reason for this sort of retirement.

In the study we also compared the rates of 'normal retirements at ages 60–64'. It is nowhere stated, as Dr Adams says, that '65 years is the normal age for retirement'. Many people retire between 60 and 64 for their own reasons, since pensions are payable after 60. We can only speculate on the reasons, and offer some suggestions.

Finally, the conclusions were reached from facts supplied by responsible parties (the employing authorities). We submit, therefore, that the accusation of a lack of objectivity is unreasonable.

Manchester Royal Infirmary,
Manchester M13 9WL
R.I. Keen
R. McNamee



RESCRIBING INFORMATION PRESENTATION Ampoules a white, opaque emulsion containing Diazepam BP 10 mg in 2 ml.

dications:

emedication before major or minor surgery or dental ocedures, endoscopy, cardiac catheterization.

Control of acute muscle spasms such as tetanus, status pilepticus and convulsions due to poisoning.

Management of severe acute anxiety or agitation including elirium tremens.

OSAGE AND ADMINISTRATION Diazemuls may be dministered by slow intravenous injection (1 ml per min), or by fusion. Diazemuls should be drawn up into the syringe mediately prior to injection.

Premedication: 0.1-0.2 mg diazepam/kg body weight by i.v. jection.

Status epilepticus: an initial dose of 0.15-0.25 mg/kg i.v. jection repeated in 30 to 60 minutes if required, and followed if ecessary by infusion of up to 3 mg/kg over 24 hours.

Tetanus: 0.1-0.3 mg diazepam/kg body weight by i.v. injection nd repeated every 1 to 4 hours as required. Alternatively, a continuous infusion of 3-10 mg/kg body weight every 24 hours may be used.

4. Anxiety and tension, acute muscle spasms, acute states of excitation, delirium tremens: The usual dose is 10 mg repeated at intervals of 4 hours as required.

Elderly or debilitated patients: Elderly and debilitated patients are particularly sensitive to the benzodiazepams. Dosage should initially be reduced to one half of the normal recommendations.

CONTRA-INDICATIONS, WARNINGS ETC. Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics or antidepressants, including MAOI's will result in accentuation of their effects. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. This should be considered where alertness is required, e.g. driving a car. As with any benzodiazepine, excessive or prolonged use may result in the development of some psychological dependence. Use with caution in patients with impairment of renal or hepatic function.

Pregnancy and Lactation: Diazepam crosses the placenta and should not be used during pregnancy unless considered essential. Large maternal doses administered during delivery may produce clinical effects in the newborn. Diazepam can be transmitted in breast milk and clinical effects may occur in the breast-fed infant.

Side effects: May rarely cause local pain or thrombophlebitis. Rare instances of a local painless erythematous rash around the site of injection, urticaria and, rarely, anaphylaxis have been reported.

Overdosage: CNS depression and coma. Treatment symptomatic.

PHARMACEUTICAL PRECAUTIONS – See Data Sheet.

Pack Size & Cost: 10 x 2 ml ampoules: NHS Price £4.40

PL: 0022/0043. Date of preparation January 1986

(Diazemuls is a registered trademark)

KabiVitrum Limited,
KabiVitrum House, Riverside Way,
Uxbridge, Middlesex UB8 2YF
Tel: Uxbridge (0895) 51144

KV647 2.87

Haemaccel®

polygeline

The flexible solution, with more than a decade of British experience

Presentation 500 ml contain 17.5 g polygeline. **Cations:** mmol/500 ml Na^+ 72.50 K^+ 2.55 Ca^{++} 3.13. **Anions:** mmol/500 ml Cl^- 72.50 PO_4^{---} and SO_4^{--} traces. pH 7.2 —7.3. Sterile distilled water to 500 ml. **Uses** As a plasma volume substitute in cases of: **1.** Hypovolaemic shock due to: *a)* Haemorrhage (visible or concealed) *b)* Burns, peritonitis, pancreatitis, crush injuries *c)* Water and electrolyte loss from persistent vomiting and diarrhoea, diseases of the kidneys and adrenals, portal vein thrombosis, ileus, diabetic coma. **2.** Fluid replacement in plasma exchange. **3.** Extra-corporeal circulation. **4.** Isolated organ perfusion. **5.** As a carrier solution for insulin. **Dosage and administration** Haemaccel should be administered intravenously in a volume approximately equal to the estimated blood loss. Normally 500 ml will be infused in not less than 60 minutes, but in emergencies Haemaccel can be rapidly infused. **Hypovolaemic shock** 500-1,000 ml Haemaccel i.v. initially. Up to 1,500 ml blood loss can be replaced entirely by Haemaccel. For between 1,500 ml and 4,000 ml blood loss, fluid replacement should be with equal volumes of Haemaccel and blood, given separately (see Pharmaceutical Precautions). For losses over 4,000 ml the separate infusions should be in the ratio two parts blood to one part Haemaccel. **Burns** At least 1 ml Haemaccel per kg body weight, multiplied by the % of body surface burned should be infused in each 24 hours for two days. **Plasma exchange** Haemaccel should be given either alone or in combination with other replacement fluids in a volume adequate to replace the plasma removed. Up to 2 litres have been given as sole replacement fluid. **Contra-indications, warnings, etc.** There are no absolute contra-indications to the use of Haemaccel. However, caution should be used in any patient likely to develop circulatory overloading. Inappropriately rapid administration of Haemaccel, especially to normovolaemic patients, may cause the release of histamine. In the event of histamine release, the infusion should be discontinued and appropriate action taken with anti-histamines etc. Histamine release may be especially hazardous in patients with known allergic conditions such as asthma. Haemaccel contains calcium ions and caution should be observed in patients being treated with cardiac glycosides. Citrated blood should *not* be mixed with Haemaccel. Haemaccel should, if possible, be warmed to body temperature before use. However, in emergencies it may be infused at ambient temperatures. **Pharmaceutical precautions** As Haemaccel contains no preservatives, any unused fluid should be discarded once a bottle has been opened. Citrated blood may be infused immediately before or after haemaccel provided there is adequate flushing of the infusion set. Date of Preparation: May 1987 Basic Hospital Price: £3.43 per 500 ml bottle PL No.: 0086/0040 Further information available on request. Hoechst U.K. Ltd., Pharmaceutical Division, Hoechst House, Salisbury Road, Hounslow, Middx.

Hoechst UK Limited,
Pharmaceutical Division,
Hoechst House,
Salisbury Road,
Hounslow,
Middlesex TW4 6JH

BEHRIN

Relative potency of propofol and thiopentone

In their correspondence about the relative potencies of propofol and thiopentone (*Anaesthesia* 1987; **42:** 317–9), Drs Grant and Mackenzie and Dr Grounds and his colleagues failed to consider an important factor in determining this relation, the speed of injection of the drug. The respondents are not quite correct to say that the method they adopted was that of Stella *et al.*,[1] in that their injection was made over 20 seconds compared with Stella's 15 seconds.

The importance of speed of injection of propofol in the production of unconsciousness was demonstrated by Rolly *et al.*[2] and is confirmed by his and our own subsequent experience. Propofol leaves the blood so quickly that although a very rapid injection of a small dose may achieve a transient blood level sufficient to cause a very short period of unconsciousness, a slower injection of the same dose may never achieve that effect. The same phenomenon was noted by early investigators of propanidid. Since thiopentone behaves differently, different dose ratios exist at different injection rates (and in different populations).

Our comparisons of propofol and methohexitone all suggest equipotency.[3–5] It would be unfortunate if insistence on the use of a large dose of propofol (e.g. 2.5 mg/kg, which produces unconsciousness for a mean duration of 7.15 minutes[6]) were to remove from clinical practice the very useful method of giving a small dose of propofol (1–1.5 mg/kg) very quickly in order to produce unconsciousness for only a minute of two whilst brief surgery is completed.

University Hospital of
South Manchester,
Withington,
Manchester

B. Kay

References

1. Stella L, Torri G, Castiglioni CL. The relative potencies of thiopentone, ketamine, propanidid, alphaxalone and diazepam. A statistical study in man. *British Journal of Anaesthesia* 1979; **51:** 119–22.
2. Rolly G, Versichelen L, Huyghe L, Mungroop H. Effect of speed of injection on induction of anaesthesia using propofol. *British Journal of Anaesthesia* 1985; **57:** 743–6.
3. Kay B, Stephenson DK. Dose-response relationship for disoprofol (ICI 35868; Diprivan). Comparison with methohexitone. *Anaesthesia* 1981; **36:** 863–7.
4. Kay B, Hargreaves J, Sivalingam T, Healy TEJ. Intravenous anaesthesia for cystoscopy: a comparison of propofol or methohexitone with alfentanil. *European Journal of Anaesthesiology* 1986; **3:** 111–20.
5. Kay B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41:** 589–95.
6. Nightingale P, Healy TEJ, Hargreaves J, McGuiness K, Kay B. Propofol in emulsion form: induction characteristics and venous sequelae. *European Journal of Anaesthesiology* 1985; **2:** 361–8.

SI units, Newtons and apples

A homely analogy of this subject may help people to understand the matter. When a small apple falls the weight (the force) of one Newton acts on the mass of 0.1 kg apple and produces an acceleration of 9.81 m/second/second (the acceleration due to gravity).

So, in the examples given, an epidural catheter breaks if a supermarket bag of 20 small apples is hung on it, while the weight of a fruit-tray (40 small apples) is needed to stop gastric regurgitation.

South Medical Centre,
2685–2nd Ave. West,
Prince Albert,
Saskatchewan S6V 5E3,
Canada

J.G. Rye

Leak detection with a capnograph

Leaks in various components of anaesthetic breathing systems are a well recognised cause of hypoventilation. This is a report of yet another cause of a leak and its clinical effects.

A 13-year-old boy (45 kg body weight) presented for appendicectomy. His lungs were ventilated manually via a Magill system after a rapid sequence induction before he was transferred to the operating room where automatic ventilation was with a Manley MP2 ventilator. The tidal volume was set at 500 ml with a fresh gas flow of 6 litres/minute to reduce the hypercapnia produced by the initial ventilation via the Magill system. Initially, the patient's end tidal carbon dioxide was 5.8%; however, in spite of the degree of hyperventilation, it did not decrease as expected. Thus the system was checked for leaks. No audible leaks were discovered but a leak of gas was felt from the Cobb tracheal tube connector. Even then the cause was not immediately evident but was identified as a small hole (1–2 sq. mm) in the weld between the two tubes that make up the connector.

Once this hole was sealed with tape the patient's end tidal carbon dioxide rapidly decreased to 4.5% and was maintained at this level with a fresh gas flow of 4.5 litres/minute. It is rather surprising that such a small defect could cause a leak sufficient to be clinically significant. However, in this case the use of a capnograph identified potentially significant hypoventilation and allowed corrective measures to be taken to prevent any clinical complications.

Royal United Hospital,
Bath BA1 3NG

D.G. Martin

Anaesthesia, 1987, Volume 42, pages 1026–1028

Book reviews

Oxygen Transport in the Critically Ill 1026
Edited by J.V. Snyder and M.R. Pinsky
Geriatric Anaesthesia. Principles and Practice 1026
Edited by C.R. Stephen and R.A.E. Assaf
Cardiovascular Actions of Anesthetics and Drugs Used in Anesthesia. 2. Regional Blood Flow and Clinical Considerations 1027
Edited by B.M. Altura and S. Halevy
600 MCQs in Anaesthesia: Clinical Practice 1027
P.J. Simpson and N.W. Goodman
Clinics in Anaesthesiology, Vol. 4 No. 4. Anesthesia and the Geriatric Patient 1028
Edited by J.A. Felts

Oxygen Transport in the Critically Ill

Edited by J.V. Snyder and M.R. Pinsky. Pp. xvi + 554. Year Book Medical Publishers, Inc., 1987. £72.00.

This excellent book reviews all aspects of oxygen transport from the lung to the mitochondrion. Bookshelves already sag under the weight of volumes that describe the physiology, pathophysiology and treatment of the lungs or circulation in the critically ill patient, but this book differs in that it attempts throughout to highlight the integration of physiological systems in the attempt to deliver an adequate supply of oxygen to its destination. The basic principles of oxygen supply and demand in the normal state are described and an introduction to pathological processes is provided with the aid of case histories in the first section of the book. A comprehensive review of regulatory mechanisms associated with oxygen transport is followed by a discussion of cellular oxygenation. The latter two-thirds of the book is concerned with clinical aspects. There is a review of the clinical evaluation of global and regional oxygen transport, and methods to support the failing respiratory and cardiovascular systems are described fully.

Perhaps because of the single theme, the book is relatively consistent throughout, despite a large number of authors. There is relatively little repetition. Each topic is discussed comprehensively, with ample illustrations in the form of diagrams, tables and case histories. Research work is reviewed critically and conclusions are balanced. Some of the authors stimulate thought by their proposals. For example, a very convincing argument is made for the re-introduction of the term 'respirator lung' because of alveolar pathology which results from inappropriate patterns of ventilation, and possible methods of its prevention are discussed. There is a very welcome emphasis on oxygen saturation and content rather than oxygen tension.

There is little to criticise in this book except for the occasional gross Americanism (e.g. 'one intuits that . . .'). It is well laid out, easy to read and understand, and refreshing in its single theme approach. The index is comprehensive and it is as up to date as one would expect of a book of its size; the most recent references are from 1985.

The editors of this volume have successfully avoided the trap of considering the body as a collection of independent physiological systems. As Dr Stephen Ayres points out in his foreword, the barrier between cardiovascular and respiratory systems was created primarily by cardiologists and chest physicians, and has proved difficult to dismantle. However, it is particularly important in the intensive care unit, where co-existing pulmonary and cardiovascular pathology is common, that such artificial barriers should be ignored. Many anaesthetists are already aware of the importance of considering the patient as a whole, and will find much valuable information in the book. However, it is a book which should be read by all who are responsible for the care of the critically ill patient.

A.R. Aitkenhead

Geriatric Anaesthesia. Principles and Practice

Edited by C.R. Stephen and R.A.E. Assaf. Pp. vii + 376. Butterworths, 1986. £39.50.

Geriatrics is a growth area, due in part to the ageing population and also the increasing political awareness of the sociomedical problems of the old. Yet it is doubtful if individual anaesthetists have noticed changes over the last decade since much of our time has always been devoted to the elderly, on whom the majority of operations are performed anyway. This is the second book on geriatrics and anaesthetics within a year. Does this herald the birth of yet another subspecialty?

The editors have attempted to draw together topics of special relevance to the elderly. However, as the elderly form so prominent a part of everyday anaesthesia, many of these topics could have been included in a general text. Five of the 15 chapters are devoted to the cardiovascular system which, though important, seems excessive when only single chapters are devoted respectively to the respiratory system, the kidneys and the brain. However, these latter three chapters are all especially well written by nonanaesthetists who, presumably, have answered the editors' call to write about the influence of age on their respective body systems.

The chapters on 'Pros and cons of regional anaesthesia' and on monitoring are not written with the geriatric patient particularly in mind. In the former chapter it is admitted that pathological status is more important than age *per se*, a view which could be repeated regularly throughout the book.

The chapter on alterations in drug disposition is detailed, well referenced and contains much that is relevant. The following chapter on drug interactions seems to be largely reprinted from 7- and 13-year-old papers respectively, and is naturally disappointing. The succeeding chapter on premedication is humdrum and descends to the level of clinical anecdote.

The book is well printed on good paper and is strongly bound. The layout is pleasing and the illustrations are mainly unambiguous and clear. The standard of chapter referencing is variable: some authors rake out the usual oldies while others provide a useful, recent and imaginative list. An index is included.

This book should be purchased by medical school libraries and by many more distant departmental libraries. Both trainees and more senior anaesthetists would benefit from reading it selectively.

F.R. Ellis

Cardiovascular Actions of Anesthetics and Drugs Used in Anesthesia. 2. Regional Blood Flow and Clinical Considerations

Edited by B.M. Altura and S. Halevy. Pp. 294. Karger, 1986. £97.80.

This is the second of two companion volumes under this title (the first was reviewed in *Anaesthesia* 1986; **41:** 1170 and 1286). This book deals with regional blood flow and clinical considerations, and considers matters by physiological system rather than by type of agent. Thus, whereas the first volume tended to deal with the effects of intravenous anaesthetics or narcotic analgesics, and so on, this volume deals with effects on coronary circulation, pulmonary circulation, renal circulation, etc. There is also a very comprehensive review of the effect of anaesthetics during shock and trauma from both the practical and theoretical points of view.

This volume is very much more enjoyable to read than Volume 1 although the reader should be aware that a great deal of current information comes from experimental studies in a variety of animals and far too little reliable data are available in normal man. This is abundantly appreciated by many of the authors. This is least true of the effects of anaesthetic agents on coronary circulation, thanks to the frequency with which invasive monitoring can justifiably be employed on patients who undergo surgery for coronary artery disease. However, once we reach areas such as the pulmonary or splanchnic circulation, there is much less direct evidence.

It would be invidious to select chapters for special mention since the general level is extremely high. However, in view of a current controversy in the United Kingdom, this reviewer would particularly commend the chapter on the effects of anaesthetics on the splanchnic circulation to those who believe that halothane is unpredictably toxic to the liver. It provides a very thoughtful analysis of the mechanisms whereby the effects might be mediated which should stimulate some challenging thoughts on how they might be mitigated or even avoided.

This volume contains good reviews of a wide range of literature on a potentially very important aspect of the pharmacology of anaesthetic agents, which in special fields is crucial to the selection of the currently optimal agent or combination of agents. However, even the generalist will find much to provoke thought as to the best conduct of anaesthesia in all sorts of situations. To what extent the theoretically best choices lead to detectably better results, must await detailed outcome studies.

M.D. Vickers

600 MCQs in Anaesthesia: Clinical Practice

By P.J. Simpson and N.W. Goodman. Pp. x + 232. Churchill Livingstone, 1987. £7.95 paperback.

As one who has faced multiple choice examinations on a number of occasions and who has not infrequently felt badly mauled, one approached this book with some trepidation. It was, therefore, pleasantly surprising to find that one's confidence in the multiple choice technique grew as one read through it. The book is a companion to a similar volume on *Basic Sciences* (reviewed in *Anaesthesia* 1986; **41:** 228) and has substantially the same format as its predecessor. Following the author's five-page introduction and guide to multiple choice, there are ten papers of 60 questions. Each paper is interposed with a section of answers presented in a true/false format, together with the occasional single-line qualifying comment. The index at the end of the book reclassifies the questions into the four major categories of anaesthesia, anatomy, medicine and surgery and then into 42 subcategories.

It is impossible to review 600 multiple choice questions. My overall impression was that the authors managed to cover the length and breadth of anaesthetic clinical practice without too much repetition. There are rather too many of the 'curse' words of multiple choice questions (may, rarely, always, commonly) but since reader and writer seemed to have the same sense of balance of these words, my personal success was satisfactory. This may not be so when faced with questions set in Parts I and III of the FFARCS examination or the European Diploma, the groups at which this book is specifically aimed.

The authors must be applauded for their efforts in their collation of 600 questions. Their recommendation is to do each paper in approximately one and a half hours and, although one's confidence in the technique grew, one actually learnt very little. Thus, individuals might resent the loss of 15 hours of valuable revision time in the immediacy of an exam to learn a technique but not to gain valuable knowledge. This book is therefore recommended for those who need practice in the multiple choice technique. It should not be regarded as a short cut for last minute examination revision.

D.A. Zideman

Clinics in Anaesthesiology, Vol. 4 No. 4. Anesthesia and the Geriatric Patient

J.A. Felts. Pp. ix + 252. W.B. Saunders Co., 1986. Annual subscription (4 vols) £35.00.

Books that depend on an editor who collates the writings of a number of authors, gain from the expertise of highly qualified individuals but may lose the continuity and theme that are found in books by a single writer. Problems are frequently restated in the individual chapters whilst important areas can go unmentioned. It is always difficult for any editor to avoid all the pitfalls. This edition of *Clinics* deals with anaesthesia and the geriatric patient and suffers, to some extent, from this problem. The editor states that he has specifically avoided chapters which discuss the ageing process and the associated physiological and pharmacological problems. However, each writer has been encouraged to outline the problems in the individual chapters. One might question the wisdom of this decision, because it is essentially these changes that create the problems with anaesthesia in the geriatric patient. Nevertheless, this edition of *Clinics* is both informative and comprehensive with realistically chosen references and is reasonably well indexed.

Several chapters are particularly well written and interesting. The chapter on thermoregulation and postoperative hypothermia is one of these, with a comprehensive text and a selection of relevant graphs from the literature. Similarly, the chapter on respiratory considerations in the elderly surgical patient includes a detailed discussion of the physiological changes in pulmonary function with age. It also deals with the increased incidence of various diseases and has some useful comments on anaesthetic management.

The management of hypertension and diabetes is discussed at length and there are chapters that deal with most forms of surgery commonly undertaken in the elderly patient, although some of what is said in these chapters applies equally well to any patient. The chapters that discuss the anaesthetic and patient management for specific types of surgery, such as orthopaedic and ophthalmic surgery, highlight the differences between American and British practice. The emphasis is often upon regional techniques, in situations where the British anaesthetist might use general anaesthesia. Another interesting difference in anaesthetic management between the United Kingdom and America, is the total lack of mention of the use of a capnograph to help in the control of carbon dioxide levels; in fact, in the book CO_2 measurement is rarely mentioned and then is achieved by insertion of an arterial cannula and intermittent blood gas sampling. Most British anaesthetists would regard normocapnia to be important in the elderly patient.

This edition of *Clinics in Anaesthesiology* will prove of interest to all practising anaesthetists because the majority of anaesthetists need to deal with the elderly patient. However, my early remarks about the slight lack of cohesion of presentation may mean that this book is more useful as a reference work than as an easy to read, comprehensive synopsis of the problems associated with anaesthesia in the elderly patient.

J.C. Edwards

How much pressure are you operating under?

The **DINAMAP*** Monitor
TELLS YOU - ACCURATELY

Controlling blood pressure during anaesthesia is your responsibility.
It's certainly no occasion to compromise on patient care.

OTHER MONITORS FAIL TO MATCH
The **DINAMAP*** Monitor
FOR ACCURACY, RELIABILITY OR SPEED

When it comes to the critical care of your patients only the best is good enough - there can be no compromise.

The **DINAMAP*** Monitor Model 1846SX meets your expectations with:

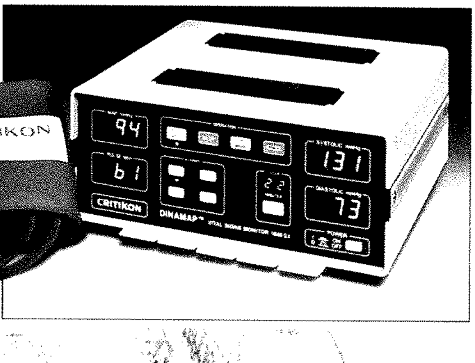
True and accurate readings:
Unique motion artefact rejection capability.
Comprehensive clinical support data.

Rapid readings:
Readings in regular mode completed in 25 seconds.
Early systolic pressure in 8 seconds flat (stat mode).

Patented cuff inflation system:
Improved patient comfort, shorter determination times.

The
DINAMAP*
Monitor

FOR NO-COMPROMISE
CRITICAL CARE



*Trademark © CRITIKON LTD 1987

CRITIKON
a Johnson & Johnson company

Broadlands Sunninghill Ascot Berkshire SL5 9JN. Telephone Ascot (0990) 27821. Telex 849423

Ultimate
performance

From Spectramed reusable
blood pressure transducers

- P10EZ range of miniature transducers
- P23XL range of standard transducers
- Extreme reliability due to new semiconductor sensor design
- Accurate over a range of −50 to +300 mm/Hg
- Pressure tolerance up to 10,000 mm/Hg
- Adaptable for use with all monitors
- Supported by a full range of pressure monitoring accessories

SPECTRAMED

Spectramed Ltd., Advanced Technology Unit II,
University of Warwick Science Park, Coventry CV4 7EZ.
Tel: Coventry (0203) 367676

Anaesthesia, 1987, Volume 42, pages 1029–1036

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for May 1987. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Irritable bowel syndrome: classification and pathogenesis. Almy, T.P., Rothstein, R.I. *Annual Review of Medicine* 1987; **38:** 257.

Surgery during acute pancreatitis. Observation in 50 patients. Choi, T.K., Ng, W.S., Wong, J. *American Journal of Surgery* 1987; **153:** 369.

Liver lesions in inflammatory bowel disorders. Desmet, V.J., Geboes, K. *Journal of Pathology* 1987; **151:** 247.

Minimizing blood transfusions during abdominal aortic surgery—recent advances in rapid autotransfusion. Hallett, J.W., Popovsky, M., Ilstrup, D. *Journal of Vascular Surgery* 1987; **5:** 601.

Mechanisms involved in colonic vasoconstriction and inhibition of motility induced by neuropeptide Y. Hellstrom, P.M. *Acta Physiologica Scandinavica* 1987; **129:** 549.

Effect of nifedipine on gastric acid secretion and gastrin release in man. McColl, K.E.L., Buchanan, N.M.M. *et al. Gut* 1987; **28:** 455.

Pharmacology

Adrenergic drugs and their antagonists

Variations of norepinephrine concentrations following chronic stressor application. Anisman, H., Irwin, H.J. *et al. Pharmacology, Biochemistry and Behavior* 1987; **26:** 653.

Noradrenaline inhibits vasoconstriction induced by electrical stimulation. Atkinson, J., Boillat, N. *et al. General Pharmacology* 1987; **18:** 219.

Early neuroleptic response: clinical profiles and plasma catecholamine metabolites. Bowers, M.B., Jr, Swigar, M.E. *et al. Journal of Clinical Psychopharmacology* 1987; **7:** 83.

Prejunctional adrenergic receptors and sympathetic neurotransmission: studies in canine skeletal muscle vasculature *in situ*. Kahan, T. *Acta Physiologica Scandinavica* 1987; **129** (Suppl. 560): 1.

Beta-blockers and lipophilicity. Leading article. *Lancet* 1987; **1:** 900.

Minireview: adrenoreceptors and the pharmacology of affective illness: a unifying theory. Lipinski, J.F., Cohen, B.M. *et al. Life Sciences* 1987; **40:** 1947.

Metabolism of alpha- and beta-adrenergic receptors *in vitro* and *in vivo*. Mahan, L.C., McKernan, R.M., Insel, P.A. *Annual Reviews of Pharmacology and Toxicology* 1987; **27:** 215.

Calorigenic action of circulating epinephrine during pentobarbital, halothane and morphine anesthesia in dogs. Sumikawa, K., Hirano, H. *et al. Research Communications in Chemical Pathology and Pharmacology* 1987; **56:** 111.

Anaesthetic agents

Effect of ketamine on local cerebral glucose utilization in fetal sleep. Abrams, R.M., Cooper, R.J. *American Journal of Obstetrics and Gynecology* 1987; **156:** 1018.

Stabilization of the reduced halocarbon–cytochrome P-450 complex of halothane by N-alkanes. Baker, M.T., Bates, J.N., Van Dyke, R.A. *Biochemical Pharmacology* 1987; **36:** 1029.

Opposing effects of anesthetics on pressure tolerance and compression rate effect. Brauer, R.W., Dutcher, J.A. *Journal of Applied Physiology* 1987; **62:** 1635.

A randomized prospective controlled study of the metabolism and hepatotoxicity of halothane in humans. Cousins, M.J., Gourlay, G.K. *et al. Anesthesia and Analgesia* 1987; **66:** 299.

Clinical pharmacokinetics of inhalational anaesthetics.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office. The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MS Dos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Dale, O., Brown, B.R., Jr. *Clinical Pharmacokinetics* 1987; **12:** 145.

Mechanisms of cerebrovascular dilation by ether in monkeys. Kang, Y.G., Nemoto, E.M. *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; **7:** 230.

Differences in diazepam pharmacokinetics in Chinese and White Caucasians—relation to body lipid stores. Kumana, C.R., Lauder, I.J. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 211.

Clinical pharmacology of benzodiazepines. Lader, M. *Annual Review of Medicine* 1987; **38:** 19.

Does isoflurane aggravate regional cerebral ischemia? Michenfelder, J.D. *Anesthesiology* 1987; **66:** 451.

Effect of ketamine on cerebral cortical blood flow and metabolism in rabbits. Oren, R.E., Rasool, N.A., Rubinstein, E.H. *Stroke* 1987; **18:** 441.

Influence of atropine upon reactivation and ageing of rat and human erythrocyte acetylcholinesterase inhibited by soman. Van Dongen, C.J., Elskamp, R.M, De Jong, L.P.A. *Biochemical Pharmacology* 1987; **36:** 1167.

Effect of inhalation anaesthetics on antipyrine pharmacokinetics of mice. Van Dyke, R.A., Kooistra, K.L. *et al. Biochemical Pharmacology* 1987; **36:** 1023.

Analgesic agents

Similar effects of acetylsalicylic acid and morphine on immediate responses to acute noxious stimulation. Hunskaar, S. *Pharmacology and Toxicology* 1987; **60:** 167.

Human pharmacology and abuse potential of meptazinol. Johnson, R.E., Jasinski, D.R. *Clinical Pharmacology and Therapeutics* 1987; **41:** 426.

Mechanographic analysis of muscle rigidity after morphine and haloperidol: a new methodological approach. Kolasiewicz, W., Baran, J., Wolfarth, S. *Naunyn-Schmiedeberg's Archives of Pharmacology* 1987; **335:** 449.

Endocrine responses to naloxone in young and old male rats. Maggi, R., Limonta, P. *et al. Neuroendocrinology Letters* 1987; **9:** 93.

Pharmacokinetics of unchanged morphine in normal and cirrhotic subjects. Mazoit, J.X., Sandouk, P. *et al. Anesthesia and Analgesia* 1987; **66:** 293.

The specificity of the pupillary actions of morphine and naloxone. Robinowitz, R., Korczyn, A.D. *Journal of Ocular Pharmacology* 1987; **3:** 17.

Muscle relaxants

Neostigmine in the antagonism of the action of atracurium. Fox, M.A., Keens, S.J., Utting, J.E. *British Journal of Anaesthesia* 1987; **59:** 468.

Pancuronium and gallamine are antagonists for pre- and post-junctional muscarinic receptors in the guinea-pig lung. Fryer, A.D., Maclagan, J. *Naunyn-Schmiedeberg's Archives of Pharmacology* 1987; **335:** 367.

Prediction of malignant hyperthermia susceptibility by clinical signs. Larach, M.G., Rosenberg, H. *et al. Anesthesiology* 1987; **66:** 547.

Role of intracellular pH in muscle fatigue. Metzger, J.M., Fitts, R.H. *Journal of Applied Physiology* 1987; **62:** 1392.

Other drugs

Cimetidine modulates natural killer cell function of patients with chronic lymphocytic leukemia. Allen, J.I., Syropoulos, H.J. *et al. Journal of Laboratory and Clinical Medicine* 1987; **109:** 396.

Pharmacokinetics in liver disease. Breimer, D.D. *Pharmaceutisch Weekblad* 1987; **9:** 79.

Osmolalities of commercially supplied drugs often used in anesthesia. Bretschneider, H. *Anesthesia and Analgesia* 1987; **66:** 361.

Hypotensive effect of bromocriptine in normal eyes. Geyer, O., Robinson, D. *et al. Journal of Ocular Pharmacology* 1987; **3:** 1.

Comparative effects of ranitidine and cimetidine on the pharmacokinetics and pharmacodynamics of warfarin in man. Toon, S., Hopkins, K.J. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 165.

Apparatus

Evaluation of a new non-invasive semiautomatic blood pressure monitoring device. Fukuoka, M., Yamori, Y. *et al. Clinical and Experimental Hypertension, Part A–Theory and Practice* 1987; **9:** 141.

Contamination control in long-term ventilation. A clinical study using a heat- and moisture-exchanging filter. Gallagher, J., Strangeways, J.E.M. *et al. Anaesthesia* 1987; **42:** 476.

Noninvasive measurements of intracardiac blood flow velocities with Doppler ultrasound. Hatle, L. *Acta Medica Scandinavica* 1987; **221:** 133.

Esophageal electrocardiography in acute cardiac care. Efficacy and diagnostic value of a new technique. Shaw, M., Niemann, J.T. *et al. American Journal of Medicine* 1987; **82:** 689.

Lower oesophageal contractility as an indicator of brain death in paralysed and mechanically ventilated patients with head injury. Sinclair, M.E., Suter, P.M. *British Medical Journal* 1987; **294:** 935.

Complications

Neurological complications following liver transplantation. Adams, D.H., Ponsford, S. *et al. Lancet* 1987; **1:** 949.

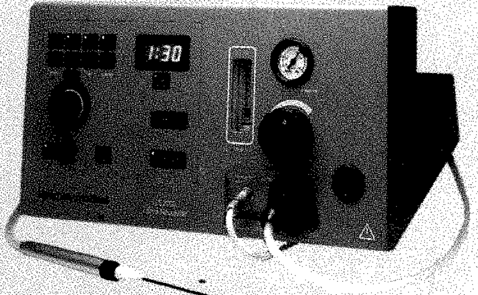
Obstructive sleep apnea initiated by a lax epiglottis.

Pain management in hospital and the home

Spembly Medical is foremost in the discipline of Pain Management. The Company has earned a unique reputation for its development of high quality instrumentation, particularly for the techniques of Cryoanalgesia and TENS.

An excellent example is the SL2000 Lloyd Neurostat. It adds a new perspective to the management of both acute and chronic pain via localised freezing of nerves. Treatment by Cryoanalgesia is of particular benefit for relieving post-operative pain and in conditions such as facet rhizolysis, coccydynia and neuroma formation.

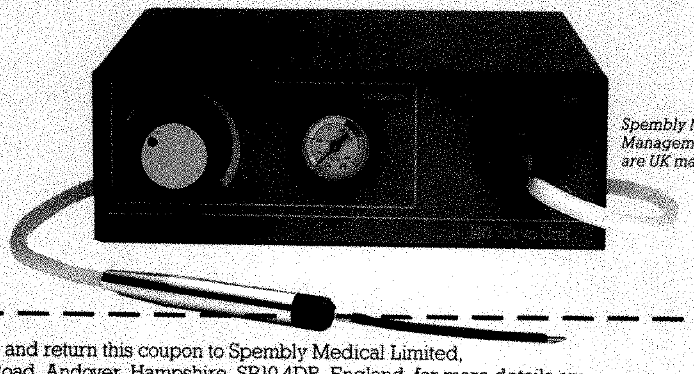
Equally, the Spembly Medical 140 Cryounit, used in conjunction with the Maiwand probe, is an established method of freezing the intercostal nerves prior to closing the thorax — a recognised means of providing post-thoracotomy pain relief.



Obtaining pain relief, without recourse to drugs, through treatment by TENS is rapidly increasing. Outstanding for this technique is the Pulsar range — a family of small, lightweight battery operated units which enable more patients to obtain greater benefits from TENS over a wider range of clinical conditions. Significantly, Spembly Medical is the first to have designed a special unit for use in Obstetrics.

Spembly medical

Spembly Medical Limited
Newbury Road, Andover, Hampshire,
SP10 4DR, England
Telephone: (0264) 65741 Telex: 47403



Spembly Medical Pain Management products are UK manufactured.

Please clip and return this coupon to Spembly Medical Limited,
Newbury Road, Andover, Hampshire, SP10 4DR, England, for more details on:— GP/A/09

☐ SL2000 Lloyd Neurostat ☐ 140 Cryounit ☐ TENS Pulsar ☐ Obstetric Pulsar

NAME .... POSITION ....

ADDRESS ....

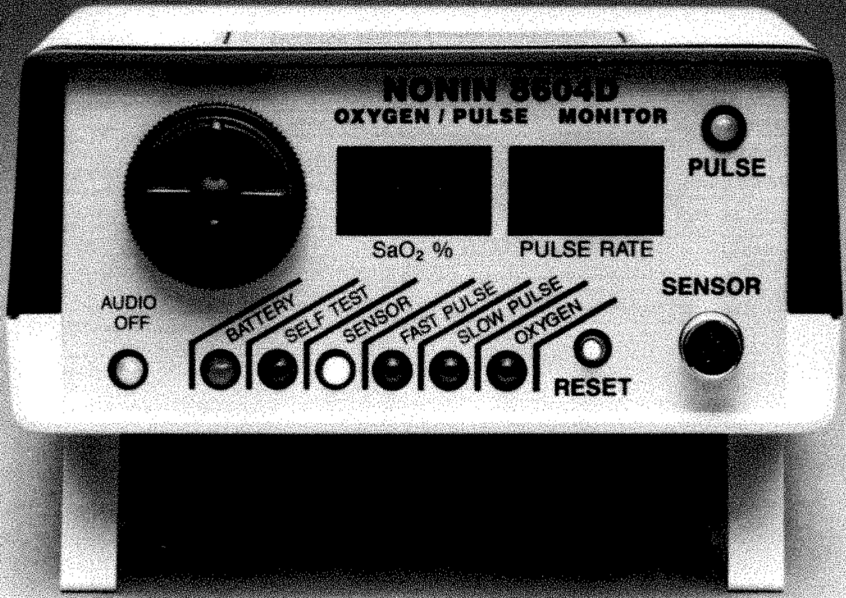
....

.... TELEPHONE ....

WHEN IT'S A MATTER OF LIFE AND BREATH

The Nonin 8604 D Pulse Oximeter

The cost effective alternative in Oximeter Technology



- Lightweight.
- Portable.
- Rechargeable Nickel Cadmium Battery.
- Wide angle digital LED readouts.
- Re-usable sensors.
- Optional continuous memory.
- Multiple data recording formats.
- Interfaceable with many playback devices.

TRIcoMED®

Tricomed Limited, Unit 2, Chiltonian Industrial Estate,
Manor Lane, London SE12 0TX
Telephone: 01-463 0933 Telex: 8955141 Trimed Fax: 01-318 0619

ANDERSEN, A.P.D., ALVING, J. *et al. Chest* 1987; **91:** 621.

Neuroleptic malignant syndrome during perphenazine treatment. NELSEN, D., AUNSHOLT, N.A., ANDERSEN, P.T. *Pharmacology and Toxicology* 1987; **60:** 221.

Left recurrent laryngeal nerve injury following internal mammary artery bypass. PHILLIPS, T.G., GREEN, G.E. *Annals of Thoracic Surgery* 1987; **43:** 440.

Hypotension and cardiac arrest in rats after infusion of mono(2-ethylhexyl) phthalate (MEHP), a contaminant of stored blood. ROCK, G. *et al. New England Journal of Medicine* 1987; **316:** 1218.

General anaesthetic procedures

Blood loss associated with uncemented total hip replacement: hypertension does not affect blood loss. WITTMAN, F.W. *Journal of The Royal Society of Medicine* 1987; **80:** 213.

General interest

Update on the diagnosis and treatment of rare neuroendocrine tumors. FRIESEN, S.R. *Surgical Clinics of North America* 1987; **67:** 379.

A phaeochromocytoma presenting with Cushing's syndrome associated with increased concentrations of circulating corticotrophin-releasing factor. JESSOP, D.S., CUNNAH, D. *et al. Journal of Endocrinology* 1987; **113:** 133.

Ondine's curse and the anaesthetist. MATHER, S.J. *Anaesthesia* 1987; **42:** 394.

Local analgesia

The effect of adrenaline in lignocaine anaesthetic solutions on plasma potassium in healthy volunteers. MEECHAN, J.G., RAWLINS, M.D. *European Journal of Clinical Pharmacology* 1987; **32:** 81.

Spinal and epidural analgesia

Epidural blood patch in the treatment of spontaneous low CSF pressure headache. GAUKROGER, P.B., BROWNRIDGE, P. *Pain* 1987; **29:** 119.

Spinal opioids

Intrathecal morphine in aortic aneurysm surgery. DAVIS, I. *Anaesthesia* 1987; **42:** 491.

Effect of substance P on cardiovascular and respiratory function in subjects. FULLER, R.W., MAXWELL, D.L. *et al. Journal of Applied Physiology* 1987; **62:** 1473.

Prolonged and biphasic respiratory depression following epidural buprenorphine. JENSEN, F.M., JENSEN, N.H. *et al. Anaesthesia* 1987; **42:** 470.

Obstetric anaesthesia and analgesia

Pulmonary injury complicating antepartum pyelonephritis. CUNNINGHAM, F.G., LUCAS, M.J., HANKINS, G.D.V. *American Journal of Obstetrics and Gynecology* 1987; **156:** 797.

Renin–angiotensin–aldosterone system and adrenergic system in hypertension induced by pregnancy—critical role of the stimulative conditions and of the lability of blood pressure in the assessment of their pathophysiological role. FIEVET, P., FOURNIER, A. *et al. Journal of Hypertension* 1986; **4** (Suppl. 5): S99.

The effect of oxytocin injection into the umbilical vein for the management of the retained placenta. KRISTIANSEN, F.V., FROST, L. *et al. American Journal of Obstetrics and Gynecology* 1987; **156:** 979.

Obstetric analgesia and fetal aortic blood flow during labour. LINDBLAD, A., BERNOW, J., MARSAL, K. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 306.

Fetal and uteroplacental haemodynamics during short-term atenolol treatment of hypertension in pregnancy. MONTAN, S., LIEDHOLM, H. *et al. British Journal of Obstetrics and Gynaecology* 1987; **94:** 312.

Maternal oxygen therapy for intrauterine growth retardation. NICOLAIDES, K.H., CAMPBELL, S. *et al. Lancet* 1987; **1:** 942.

Dose-dependent effects of prostaglandin D2 on hemodynamics, renal function, and blood gas analyses. RAO, P.S., CAVANAGH, D. *et al. American Journal of Obstetrics and Gynecology* 1987; **156:** 843.

Beta blockers in pregnancy. RUBIN, P.C. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 292.

Pre-oxygenation and the parturient patient. RUSSELL, G.N., SMITH, C.L. *et al. Anaesthesia* 1987; **42:** 346.

Anatacid therapy for emergency Caesarean section. THORBURN, J., MOIR, D.D. *Anaesthesia* 1987; **42:** 352.

Thrombotic microangiopathy in pregnancy and the postpartum period. WEINER, C.P. *Seminars in Hematology* 1987; **24:** 119.

Paediatric anaesthesia and intensive care

Gas trapping with high-frequency ventilation—jet versus oscillatory ventilation. BANCALARI, A., GERHARDT, T. *et al. Journal of Pediatrics* 1987; **110:** 617.

Surgical treatment of pediatric cardiac arrhythmia. CAMPBELL, R.M., HAMMON, J.W. *et al. Journal of Pediatrics* 1987; **110:** 501.

Effect of racemic epinephrine on ventilatory function in the neonate postextubation. COURTNEY, S.E., WACHTL, J.R. *et al. Pediatric Research* 1987; **21:** 381.

The effects of intermittent positive pressure ventilation on cerebral arterial and venous blood velocities in the new born infant. COWAN, F., THORESEN, M. *Acta Paediatrica Scandinavica* 1987; **76:** 239.

Intratracheal suctioning in sick preterm infants—prevention of intracranial hypertension and cerebral hypoperfusion by muscle paralysis. Fanconi, S., Duc, G. *Pediatrics* 1987; **79**: 538.

Elevated fetal hemoglobin levels in sudden infant death syndrome. Giuliann, G.G., Gilbert, E.F., Moss, R.L. *New England Journal of Medicine* 1987; **316**: 1122.

Diaphragmatic work of breathing in premature human infants. Guslits, B.G., Gaston, S.E. *et al. Journal of Applied Physiology* 1987; **62**: 1410.

Analgesia in the neonate. Hatch, D.J. *British Medical Journal* 1987; **294**: 920.

A simple method of face mask resuscitation at birth. Hoskyns, E.W., Milner, A.D., Hopkin, I.E. *Archives of Disease in Childhood* 1987; **62**: 376.

Pulse oximetry—an alternative method for the assessment of oxygenation in newborn infants. Jennis, M.S., Peabody, J.L. *Pediatrics* 1987; **79**: 524.

Transepidermal water loss during sleep in infants. Kahn, A., Rebuffat, E. *et al. Sleep* 1987; **10**: 111.

Postoperative apnea in preterm infants. Kurth, C.D., Spitzer, A.R. *et al. Anesthesiology* 1987; **66**: 483.

Fetal arginine vasopressin under basal and hypo-osmolal conditions. Leake, R.D., Ervin, M.G. *et al. Biology of the Neonate* 1987; **51**: 204.

Pulmonary function in the sick newborn infant. McCann, E.M., Goldman, S.L., Brady, J.P. *Pediatric Research* 1987; **21**: 313.

Maternal and fetal outcome in neonatal lupus erythematosus. McCune, A.B., Weston, W., Lee, L.A. *Annals of Internal Medicine* 1987; **106**: 518.

Comparative aspect of neonatal respiratory mechanics. Mortola, J.P. In: Benchetrit, G. *et al.*, eds. *Concepts and formalizations in the control of breathing*. Manchester: Manchester University Press, 1987; p. 287.

Dynamic trend monitoring of cerebral blood flow velocity in newborn infants. Patrinos, M.E., Muraskas, J. *et al. Journal of Pediatrics* 1987; **110**: 611.

Fetal beta-endorphin levels in response to reductions in uterine blood flow. Skillman, C.A., Clarke, K.E. *Biology of the Neonate* 1987; **51**: 217.

Ten centre trial of artificial surfactant (artificial lung expanding compound) in very premature babies. Ten Centre Study Group. *British Medical Journal* 1987; **294**: 991.

Changes in fetal and maternal blood levels of prolactin, cortisol, and cortisone during eutocic and dystocic childbirth. Van Cauwenberge, J.R., Hustin, J. *et al. Hormone Research* 1987; **25**: 125.

Effects of halothane, isoflurane and enflurane on ventilation in children. Wren, W.S., Allen, P. *et al. British Journal of Anaesthesia* 1987; **59**: 399.

The postnatal development and growth of the human lung. II. Morphology. Zeltner, T.B., Burri, P.H. *Respiration Physiology* 1987; **67**: 269.

The postnatal development and growth of the human lung. I. Morphometry. Zeltner, T.B., Caduff, J.H. *et al. Respiration Physiology* 1987; **67**: 247.

Cyclic variation in fetal heart rate and sympathetic activity. Zhu, Y.S., Szeto, H.H. *American Journal of Obstetrics and Gynecology* 1987; **156**: 1001.

Cardiovascular system

Physiology

Decreasing hydrostatic pressure does not uniformly decrease high-pressure pulmonary edema. Ali, J., Duke, K. *Chest* 1987; **91**: 588.

Ketanserin and the arterial baroreceptor reflex in normotensive subjects. Berdeaux, A., Edouard, A. *et al. European Journal of Clinical Pharmacology* 1987; **32**: 27.

The endogenous mediator of endotoxic shock. Beutler, B., Cerami, A. *Clinical Research* 1987; **35**: 192.

Why patients with congestive heart failure die: arrhythmias and sudden cardiac death. Bigger, J.T., Jr. *Circulation* 1987; **75** (Suppl.): IV-28.

Ventricular performance related to transmural filling pressure in clinical cardiac tamponade. Boltwood, C.M., Jr. *Circulation* 1987; **75**: 941.

The myocardium in ankylosing spondylitis. Brewerton, D.A., Gibson, D.G. *et al. Lancet* 1987; **1**: 995.

Mechanisms of local noradrenaline release in acute myocardial ischemia. Carlsson, L. *Acta Physiologica Scandinavica* 1987; **129** (Suppl. 559): 1.

Mechanisms of cardiac pain. Davies, G.J. In: Maseri, A. *et al.*, eds. *Hammersmith cardiology workshop series, Vol. 3*. New York: Raven Press, 1987; p. 5.

Blood viscosity in patients with bone fractures and long term bed-rest. Ernst, E., Schmidt-Pauly, E. *et al. British Journal of Surgery* 1987; **74**: 301.

Hepatic arterial pressure–flow autoregulation is adenosine mediated. Ezzat, W.R., Lautt, W.W. *American Journal of Physiology* 1987; **252** (Part 2): H836.

Electrical activity in the heart during hyperkalemic hypothermic cardioplegic arrest: site of origin and relationship of specialized conduction tissue. Ferguson, T.B., Jr., Smith, L.S. *et al. Annals of Thoracic Surgery* 1987; **43**: 373.

Baroreceptor function in congestive heart failure: effect on neurohumoral activation and regional vascular resistance. Hirsch, A.T., Dzau, V.J., Creager, M.A. *Circulation* 1987; **75** (Suppl.): IV-36.

The physiology of transferrin and transferrin receptors. Huebers, H.A., Finch, C.A. *Physiological Reviews* 1987; **67**: 520.

Cerebral blood flow and autoregulation during hypothermic cardiopulmonary bypass. Johnsson, P., Messeler, L. *et al. Annals of Thoracic Surgery* 1987; **43**: 386.

Assessment of perfusion in postoperative patients using tissue oxygen measurements. Jonnsson, K., Jensen, J.A. *et al. British Journal of Surgery* 1987; **74:** 263.

Mechanism of isoproterenol induced myocardial damage. Kondo, T., Ogawa, Y. *et al. Cardiovascular Research* 1987; **21:** 248.

Role of fibrinolysis in thrombotic thrombocytopenic purpura. Kwaan, H.C. *Seminars in Hematology* 1987; **24:** 101.

Atrial natriuretic peptide levels during development of chronic heart failure after myocardial infarction in rats. Lee, R.W., Gay, R.G. *et al. Life Sciences* 1987; **40:** 2025.

Effects of positive end-expiratory pressure on hepatic blood flow and performance. Matuschak, G.M., Pinsky, M.R., Rogers, R.M. *Journal of Applied Physiology* 1987; **62:** 1377.

Impairment of cardiopulmonary baroreflex after cardiac transplantation in human. Mohanty, P.K., Thames, M.D. *et al. Circulation* 1987; **75:** 914.

Atrial natriuretic peptide correlates with pulmonary arterial pressure and cardiac output. Naruse, K., Naruse, M. *et al. Peptides* 1987; **8:** 285.

Role of neurohormonal mechanisms in determining survival in patients with severe chronic heart failure. Packer, M., Lee, W.H. *et al. Circulation* 1987; **75** (Suppl.): IV-80.

Influence of cardiopulmonary receptors on the bradycardic responses to carotid baroreceptor stimulation in man. Parati, G., Grassi, G. *et al. Clinical Science* 1987; **72:** 639.

Atrial natriuretic factor—a possible link between left atrium, plasma volume, adrenergic control and renin–aldosterone in mitral valve prolapse. Pasternac, A., Kouz, S. *et al. Journal of Hypertension* 1986; **4** (Suppl. 5): S76.

Sleep deprivation and cardiorespiratory function—influence of intermittent submaximal exercise. Plyley, M.J., Shephard, R.J. *et al. European Journal of Applied Physiology* 1987; **56:** 338.

The effect of low-flow cardiopulmonary bypass on cerebral function: an experimental and clinical study. Rebeyka, I.M., Coles, J.G. *et al. Annals of Thoracic Surgery* 1987; **43:** 391.

Atrial natriuretic hormone is not elevated during dopamine induced natriuresis. Shenker, Y., Weder, A.B., Grekin, R.J. *Life Sciences* 1987; **40:** 1965.

Myocardial ischemia and arrhythmias. Sheridan, D.J. In: Maseri, A. *et al.*, eds. *Hammersmith cardiology workshop series, Vol. 3.* New York: Raven Press, 1987; p. 133.

Hemodynamic characteristics of sodium-sensitive human subjects. Sullivan, J.M., Prewitt, R.L. *et al. Hypertension* 1987; **9:** 398.

Serotonin and the blood-vessel wall. Vanhoutte, P.M. *Journal of Hypertension* 1986; **4** (Suppl. 5): S112.

Effects of hypoxia, hyperkalemia, and metabolic acidosis on canine subendocardial action potential conduction. Veenstra, R.D., Joyner, R.W. *et al. Circulation Research* 1987; **60:** 93.

Hormonal responses and blood pressure maintenance in normal and hypertensive subjects during acute blood loss. Velasquez, M.T., Menitove, J.E. *et al. Hypertension* 1987; **9:** 423.

Muscle sympathetic activity and venous plasma noradrenaline concentrations during static exercise in normotensive and hypertensive subjects. Wallin, B.G., Morlin, C., Hjemdahl, P. *Acta Physiologica Scandinavica* 1987; **129:** 489.

Treatment and medication

Mechanism of direct cardiostimulating actions of hydralazine. Azuma, J., Sawamura, A. *et al. European Journal of Pharmacology* 1987; **135:** 137.

Clinical pharmacology of ramipril. Ball, S.G., Robertson, J.I.S. *American Journal of Cardiology* 1987; **59:** 23D.

Ramipril: review of pharmacology. Becker, R.H.A., Scholkens, B. *American Journal of Cardiology* 1987; **59:** 3D.

Use of hypertonic saline in the treatment of hemorrhagic shock. Bitterman, H., Triolo, J., Lefer, A.M. *Circulatory Shock* 1987; **21:** 271.

The effect of blood pretransfusion on orthotopic cardiac transplantation. Keogh, A., Baron, D.W. *et al. Transplantation Proceedings* 1987; **19:** 2845.

Underlying cardiac lesions in adults with infective endocarditis. The changing spectrum. McKinsey, D.S., Ratts, T.E., Bisno, A.L. *American Journal of Medicine* 1987; **82:** 681.

Pharmacokinetic prediction of serum digoxin concentration in the elderly. Mooradian, A.D., Wynn, E.M. *Archives of Internal Medicine* 1987; **147:** 650.

Prognostic stratification of patients after myocardial infarction. Murray, D.P., Salith, M. *et al. British Heart Journal* 1987; **57:** 313.

Imidazole and indomethacin improve hepatic perfusion in sepsis. Schirmer, W.J., Schirmer, J.M. *et al. Circulatory Shock* 1987; **21:** 253.

Effectiveness of low-dose heparin in prevention of myocardial reinfarction. Semeri, G.G.N., Rovelli, F. *et al. Lancet* 1987; **1:** 937.

Impact of a trauma system on outcome of severely injured patients. Shackford, S.R., Mackersie, R.C. *et al. Archives of Surgery* 1987; **122:** 523.

Effects of low-dose cyclosporine A on toxicity and rejection in cardiac transplantation. Spratt, P., Ensmore, D. *et al. Transplantation Proceedings* 1987; **19:** 2847.

Beta-adrenergic blocking agents in the treatment of hypertension—choices based on pharmacological properties and patient characteristics. Wallin, J.D., Shah, S.V. *Archives of Internal Medicine* 1987; **147:** 654.

Suppression of shivering decreases oxygen consumption and improves hemodynamic stability during postoperative rewarming. Zwischenberger, J.B., Kirsh, M.M. *et al. Annals of Thoracic Surgery* 1987; **43:** 428.

Respiration

Physiology

Mitochondrial transmembrane potential and pH gradient during anoxia. Andersson, B.S., Aw, T.Y., Jones, D.P. *American Journal of Physiology* 1987; **252** (Part 1): C349.

Mitochondrial transmembrane ion distribution during anoxia. Aw, T.Y., Andersson, B.S., Jones, D.P. *American Journal of Physiology* 1987; **252** (Part 1): C356.

Suppression of mitochondrial respiratory function after short-term anoxia. Aw, T.Y., Andersson, B.S., Jones, D.P. *American Journal of Physiology* 1987; **252** (Part 1): C362.

Respiratory load-compensating mechanisms in muscular dystrophy. Axen, K., Bishop, M., Haas, F. *Journal of Applied Physiology* 1987; **62:** 1647.

Changes in lung volume and breathing pattern during exercise and CO_2 inhalation in humans. Cha, E.J., Sedlock, D., Yamashiro, S.M. *Journal of Applied Physiology* 1987; **62:** 1544.

Synaptic and non-synaptic mechanisms involved in the central generation and control of breathing. Denavit-Saubie, M., Champagnat, J. *et al.* In: Benchetrit, G. *et al.*, eds. *Concepts and formalizations in the control of breathing.* Manchester: Manchester University Press, 1987; p. 233.

Effects of thoracoabdominal breathing patterns on inspiratory effect sensation. Fitting, J.W., Chartrand, D.A. *et al. Journal of Applied Physiology* 1987; **62:** 1665.

Effects of norepinephrine and fluid administration on diaphragmatic O_2 consumption in septic shock. Hussain, S.N.A., Rutledge, F. *et al. Journal of Applied Physiology* 1987; **62:** 1368.

Muscle O_2 deficit during hypoxia and two levels of O_2 demand. King, C.E., Dodd, S.L., Cain, S.M. *Journal of Applied Physiology* 1987; **62:** 1384.

Delayed resolution of high-pressure pulmonary edema or capillary leak. Mayers, I., Stimpson, R., Oppenheimer, L. *Surgery* 1987; **101:** 450.

Oscillatory changes in ventilation, awake and asleep. Pack, A.I., Millman, R.P. *et al.* In: Benchetrit, G. *et al.*, eds. *Concepts and formalizations in the control of breathing.* Manchester: Manchester University Press, 1987; p. 299.

The metabolic function of the lung. Wunands, W.J.A. *Pharmaceutisch Weekblad* 1987; **9:** 61.

Effect of hyperinflation and equalization of abdominal pressure on diaphragmatic action. Zocchi, L., Garzaniti, N. *et al. Journal of Applied Physiology* 1987; **62:** 1655.

Treatment and medication

The history of the use of alcohol in the treatment of respiratory disease. Ayres, J.G. *British Journal of Diseases of the Chest* 1987; **81:** 80.

Salbutamol and ipratropium in partially reversible airway obstruction. Connolly, C.K., Chan, N.S. *British Journal of Diseases of the Chest* 1987; **81:** 55.

Barotrauma: pathophysiology, risk factors, and prevention. Haake, R., Schlichtig, R. *et al. Chest* 1987; **91:** 608.

Prophylactic effect of aminophylline and salbutamol on histamine-induced bronchoconstriction. Jones, J.G., Jordan, C. *et al. British Journal of Anaesthesia* 1987; **59:** 498.

Cardiac dysrhythmia following pneumonectomy; clinical correlates and prognostic significance. Krowka, M.J., Pairolero, P.C. *et al. Chest* 1987; **91:** 490.

Prediction of successful ventilator weaning using airway occlusion pressure and hypercapnic challenge. Montgomery, A.B., Holle, R.H.O. *et al. Chest* 1987; **91:** 496.

Practical problems in the respiratory care of patients with muscular dystrophy. Smith, P.E.M., Calverley, P.M.A. *et al. New England Journal of Medicine* 1987; **316:** 1197.

Central nervous system

Physiology

Hysterical paraplegia. Baker, J.H., Silver, J.R. *Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50:** 375.

Biochemistry and physiology of brain ammonia. Cooper, A.J.L., Plum, F. *Physiological Reviews* 1987; **67:** 440.

The effect of anxiety on cortical cerebral blood flow and metabolism. Gur, R.C., Gur, R.E. *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; **7:** 173.

Intra-cerebral recordings of the primary auditory evoked potentials in man. Liegeoischauvel, C., Chauvel, P. *et al.* In: Engel, J. *et al.*, eds. *Fundamental mechanisms of human brain function.* New York: Raven Press, 1987; p. 39.

The neuropsychology of moderate head injury. McMillan, T.M., Glucksman, E.E. *Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50:** 393.

Effect of aging on sleep-related changes in respiratory variables. Naifeh, K.H., Severinghaus, J.W., Kamiya, J. *Sleep* 1987; **10:** 160.

Regulation of the microenvironment of peripheral nerve; role of the blood–nerve barrier. Rechthand, E., Rapoport, S.I. *Progress in Neurobiology* 1987; **28:** 303.

Acetylcholine and the regulation of REM sleep: basic mechanisms and clinical implications for affective illness and narcolepsy. SHIROMANI, P.J., GILLIN, J.C., HENRIKSEN, S.J. *Annual Review of Pharmacology and Toxicology* 1987; **27:** 137.

Mechanism for the hypotestosteronemia of the sleep apnea syndrome. WORTSMAN, J., EAGLETON, L.E. *et al. American Journal of the Medical Sciences* 1987; **293:** 221.

Treatment and medication

Reduction of experimental intracranial hypertension by lidocaine. EVANS, D.E., KOBRINE, A.I. *Neurosurgery* 1987; **20:** 542.

Trial of a dopaminergic antidepressant in obstructive sleep apnea. GEORGE, C.F., WEST, P. *et al. Sleep* 1987; **10:** 180.

Effect of lidocaine treatment on acute spinal cord injury. HAGHIGHI, S.S., CHEHRAZI, B.B. *et al. Neurosurgery* 1987; **20:** 536.

High-dose acetylsalicylic acid after cerebral infarction. HLEMERS, C. *Stroke* 1987; **18:** 325.

Vertebrobasilar insufficiency. 2. Microsurgical treatment of intracranial vertebrobasilar disease. HOPKINS, L.N., MARTIN, N.A. *et al. Journal of Neurosurgery* 1987; **66:** 662.

Vertebrobasilar insufficiency. 1. Microsurgical treatment of extracranial vertebrobasilar disease. SPETZLER, R.F., HADLEY, M.N. *et al. Journal of Neurosurgery* 1987; **66:** 648.

Endocrine and metabolic

Physiology

Morphological changes in the renal macula densa during natriuresis and diuresis. ALCORN, D., ANDERSON, W.P., RYAN, G.B. *Renal Physiology* 1986; **9:** 335.

Effect of oral morphine and naloxone on pituitary-adrenal response in man induced by human corticotropin-releasing hormone. ALLOLIO, B., SCHULTE, H.M. *et al. Acta Endocrinologica* 1987; **114:** 509.

Muscle chloride channels. BRETAG, A.H. *Physiological Reviews* 1987; **67:** 618.

Histaminergic neuromodulation of the release of vasopressin. CACABELOS, R., YAMATODANI, A. *et al. Neuroendocrinology* 1987; **45:** 368.

Plasma corticotropin-releasing hormone concentrations during pregnancy and parturition. CAMPBELL, E.A., LINTON, E.A. *et al. Journal of Clinical Endocrinology and Metabolism* 1987; **64:** 1054.

Effect of stimulation of afferent renal nerves on plasma levels of vasopressin. CAVERSON, M.M., CIRIELLO, J. *American Journal of Physiology* 1987; **252** (Part 2): R801.

Role of calcium in effects of atrial natriuretic peptide on aldosterone production in adrenal glomerulosa cells. CHARTIER, L., SCHIFFRIN, E.L. *American Journal of Physiology* 1987; **252** (Part 1): E485.

Loss of spontaneous variability of fingertip anastomotic blood flow in diabetic autonomic neuropathy. CORCORAN, J.S., YUDKIN, J.S. *Clinical Science* 1987; **72:** 557.

Increased serum aldosterone in diabetic pregnancy. CUGINI, P., LETIZIA, C. *et al. Diabetologia* 1987; **30:** 169.

Effects of atrial natriuretic factor on hormone-induced renin release. DERAY, G., BRANCH, R.A. *et al. Hypertension* 1987; **9:** 513.

Electro-mechanical failures and lactate production during fatigue. DUCHATEAU, J., DEMONTIGNY, L., HAINAUT, K. *European Journal of Applied Physiology* 1987; **56:** 287.

Diabetes insipidus in pregnancy associated with abnormally high circulating vasopressinase activity. DURR, J.A., HOGGARD, J.G. *et al. New England Journal of Medicine* 1987; **316:** 1070.

Kinetics of insulin disappearance from plasma in cortisone-treated normal subjects. ELLEMANN, K., THORSTEINSSON, B. *et al. Clinical Endocrinology* 1987; **26:** 623.

Levodopa pharmacokinetic mechanisms and motor fluctuations in Parkinson's disease. FABBRINI, G., JUNCOS, J. *et al. Annals of Neurology* 1987; **21:** 370.

Calcium channels and calcium channel antagonists. GREENBERG, D.A. *Annals of Neurology* 1987; **21:** 317.

Pathogenesis of clinical hyponatremia: observations of vasopressin and fluid intake in 100 hyponatremic medical patients. GROSS, P.A., PEHRISCH, H. *et al. European Journal of Clinical Investigation* 1987; **17:** 123.

Acute natriuretic effect of nifedipine in hypertensive patients and normotensive controls—a proximal tubular effect. KRUSELL, L.R., CHRISTENSEN, C.K., PEDERSEN, O.L. *European Journal of Clinical Pharmacology* 1987; **32:** 121.

Correlation between osmoregulation and cell volume regulation. LANG, M.A. *American Journal of Physiology* 1987; **252** (Part 2): R768.

Effect of lithium on the metabolic response to parathyroid hormone. LAZARUS, J.H., DAVIES, C.J. *et al. Mineral and Electrolyte Metabolism* 1987; **13:** 63.

Renal hemodynamic effects of calcium antagonists. LOUTZENHISER, R.D., EPSTEIN, M. *American Journal of Medicine* 1987; **82:** 23.

Volume regulatory loss of Na, Cl, and K from rat brain during acute hyponatremia. MELTON, J.E., PATLAK, C.S. *et al. American Journal of Physiology* 1987; **252** (Part 2): F661.

Growth hormone secretion—neuropharmacological aspects. MULLER, E.E., CELLA, S.G. *et al.* In: LEDECKE, D.K., TOLIS, G., eds. *Growth hormone, growth factors, and acromegaly.* New York: Raven Press, 1987; p. 55.

Effects of atrial natriuretic peptide, dopamine, and ouabain on aldosterone synthesis. NAKAJIMA, S., SUZUKI, H. *et al. Acta Endocrinologica* 1987; **115:** 57.

Pituitary-adrenocortical response to metoclopramide in patients with acromegaly and prolactinoma: a clinical evaluation of catecholamine-mediated ACTH secretion. NISHIDA, S., MATSUKI, M. *et al. Journal of Clinical Endocrinology and Metabolism* 1987; **64:** 995.

Lack of effect of atrial natriuretic peptide on vasopressin release. OGAWA, K., ARNOLDA, L.F. *et al. Clinical Science* 1987; **72:** 525.

Beta-endorphin and ACTH in plasma: effects of physical and psychological stress. OLTRASS, C.M., MORA, F., VIVES, F. *Life Sciences* 1987; **40:** 1683.

Somatostatin. PATEL, Y.C. In: LUDECKE, D.K., TOLIS, G., eds. *Growth hormone, growth factors, and acromegaly.* New York: Raven Press, 1987; p. 21.

Effects of adenosine infusion into renal interstitium on renal hemodynamics. PAWLOWSKA, D., GRANGER, J.P., KNOX, F.G. *American Journal of Physiology* 1987; **252** (Part 2): F678.

Amino acid clearance in cirrhosis: a predictor of postoperative morbidity and mortality. PEARL, R.H., CLOWES, G.H.A., JR. *et al. Archives of Surgery* 1987; **122:** 468.

Glucocorticoid inhibition of neurohypophysial vasopressin secretion. RAFF, H. *American Journal of Physiology* 1987; **252** (Part 2): R635.

Alterations of water, electrolyte and acid–base homeostasis in the alcoholic. SCHAEFER, R.M., TESCHNER, M., HEIDLAND, A. *Mineral and Electrolyte Metabolism* 1987; **13:** 1.

Evidence against a pressor role for vasopressin in spontaneous hypertension. SLADEK, C.D., BLAIR, M.L., MANGIAPANE, M. *Hypertension* 1987; **9:** 332.

Binding sites for atrial natriuretic factor (ANF) in kidneys and adrenal glands of spontaneously hypertensive (SHR) rats. SWITHERS, S.E., STEWART, R.E., MCCARTY, R. *Life Sciences* 1987; **40:** 1673.

Effect of insulin on osmoregulation of vasopressin. VOKES, T.P., AYCINENA, P.R., ROBERTSON, G.L. *American Journal of Physiology* 1987; **252** (Part 1): E538.

Treatment and medication

Natriuretic factors—new concepts and perspectives in kidney disease. CLARKSON, E.M. In: DAMICO, G., COLASANTI, G., eds. *New perspectives in diagnosis and treatment of kidney disease.* Basel: Karger AG, 1987; p. 60.

Captopril attenuates diuretic and natriuretic actions of furosemide but not atrial natriuretic peptide. DI NICOLANTONIO, R., MORGAN, T.O. *Clinical and Experimental Hypertension, Part A—Theory and Practice* 1987; **9:** 19.

Shock wave lithotripsy. DISILVERIO, F., GALUCCI, M. In: DAMICO, G., COLASANTI, G., eds. *New perspectives in diagnosis and treatment of kidney disease.* Basel: Karger AG, 1987; p. 94.

Malignant somatostatinoma presenting with diabetic ketoacidosis. JACKSON, J.A., RAJU, B.U. *et al. Clinical Endocrinology* 1987; **26:** 609.

Subcutaneous tissue oxygen tension falls during hemodialysis. JENSEN, J.A., GOODSON, W.H. *et al. Surgery* 1987; **101:** 416.

Pathophysiology and clinical aspects of drug-induced tubular necrosis in man. KLEINKNECHT, D., LANDAIS, P., GOLDFARB, B. In: DAMICO, G., COLASANTI, G., eds. *New perspectives in diagnosis and treatment of kidney disease.* Basel: Karger AG, 1987; p. 145.

Potassium-lowering effect of albuterol for hyperkalemia in renal failure. MONTOLIU, J., LENS, X.M., REVERT, L. *Archives of Internal Medicine* 1987; **147:** 713.

Effect of oral frusemide on diagnostic indices of thyroid function. NEWNHAM, H.H., HAMBLIN, P.S. *et al. Clinical Endocrinology* 1987; **26:** 423.

Pain

Treatment and medication

Pain on a surgical ward: a survey of the duration and intensity of pain and the effectiveness of medication. MELZACK, R., ABBOTT, F.V. *et al. Pain* 1987; **29:** 67.

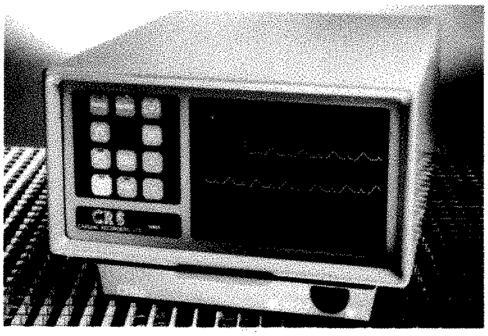
Role of cryoanalgesia in the control of pain after thoracotomy. ROXBURGH, J.C., MARKLAND, C.G. *et al. Thorax* 1987; **42:** 292.

Efficacy of diclofenac in a single prophylactic dose in postoperative pain. TIGERSTEDT, L., JANHUNEN, L., TAMMISTO, T. *Annals of Clinical Research* 1987; **19:** 18.

Other

Treatment and medication

Management of increased intraocular pressure after cataract extraction. RUIZ, R.S., WILSON, C.A. *et al. American Journal of Ophthalmology* 1987; **103:** 487.



CR6 High Performance Monitor From Cardiac Recorders

Cardian III CR6 is a NEW monitor range especially designed for use in CCU, ITU, SCBU and Theatres.

Monitoring Parameters available are - ECG, BP/PP, Respiration, 2 Temperatures PLUS access to trends of all parameters over 0.5, 2, 8, 24 Hours.

A unique feature of Cardian III is the "30 second scroll back", enabling the user to search back up to 30 secs. for a particular Arrhythmia, Freeze and Record if required.

For further details please contact:

Cardiac Recorders Ltd,
34 Scarborough Road,
London, N4 4LU
Tel: 01-272 9212/7 **Telex: 297352 CARDIA G**

THE UNIVERSITY OF BIRMINGHAM
FACULTY OF MEDICINE AND DENTISTRY
BOARD OF GRADUATE CLINICAL STUDIES

Preparation in the

West Midlands Region

for the 1987–88

PART III F.F.A.R.C.S. EXAMINATIONS

Course Co-ordinator: **Dr J W Freeman, Prof. P Hutton**

A comprehensive and systematic course of lectures, tutorials and demonstrations has been compiled to prepare candidates for this examination. These will be full time, instructional blocks and candidates can apply for any individual course or combination of courses shown below. It has been organised in this manner so that people can optimise their preparation for both the January and May examinations. Speakers on all courses will be drawn from throughout the West Midlands, with some lectures being given by national experts.

GENERAL ANAESTHESIA AND INTENSIVE CARE (Including Clinical Measurement and Pharmacology). *Fee* **£250**
7th–18th Sept. incl. *Venue:* **Queen Elizabeth Hospital Post Graduate Centre**

LOCAL ANAESTHETIC TECHNIQUES AND PAIN RELIEF. *Fee* **£75**
2nd–4th Nov. incl. *Venue:* **East Birmingham Hospital Post Graduate Centre**
Repeated with similar material: **13th–15th April incl. 1988.** *Venue:* **Alexandra Hospital, Redditch**

FINAL PREPARATION COURSE (X-Rays, Ecgs, Tutorials, Vivas) *Fee* **£75**
9th–11th Dec. incl. *Venue:* **Queen Elizabeth Hospital Post Graduate Centre**
Repeated with similar material: **13th–15th June incl. 1988.** *Venue:* **Walsgrave Hospital, Coventry**

To facilitate booking, please apply at least four weeks prior to the course starting date if possible. All fees include lunch and refreshments. *For further details please contact* **Miss D Moody, University Department of Anaesthetics, Queen Elizabeth Hospital, Birmingham B15 2TH. Tel. 021 472 1301 Ext. 2402**

Publications of Interest to ANESTHESIOLOGISTS

Indispensable tools for maintaining professional competency

ANESTHESIOLOGY

Journal of the American Society of Anesthesiologists, Inc.

Lawrence J. Saidman, M.D., Editor-in-Chief

Anesthesiologists nationwide look to this distinguished journal for current information on all facets of anesthesiology: pharmacologic bases of anesthesia; clinical principles, practices, and techniques; anesthesia management; complications of anesthesia and surgery; and more. The information is published in articles, reviews, current comments, editorial views, case reports, abstracts of current literature, and book reviews.

Published monthly. Individual rate $30.00 per year (U.S.), $69.00 (elsewhere).

REGIONAL ANESTHESIA

Journal of the American and European Societies of Regional Anesthesia

Phillip O. Bridenbaugh, M.D., Editor

For the growing number of those concerned with the burgeoning specialty of regional and local anesthesia, this quarterly journal publishes highly informative articles on the clinical applications of current research and on professional issues and developments.

In addition to original articles, regular features include review articles discussing the current status of particular facets of the field; abstracts from other journals, especially international publications; case reports; clinical reports; correspondence; announcements of professional events; and editorials.

Highlights each year include the full text of the Labat Address, focusing on the humane and philosophical foundations of this field; and the Abbott Lecture, a scholarly and lively look at a particular aspect of regional and local anesthesia and its present implications.

Published quarterly. Individual rate $37.00 (U.S.), $41.00 (elsewhere). Residents $25.00 (U.S. only).

ASA Refresher Courses in Anesthesiology

A Project in the Continuing Education Program of the American Society of Anesthesiologists

Paul Barash, M.D., Editor

Each annual volume in this popular series consists of thirteen to seventeen complete and edited lectures selected from regional and national ASA Refresher Courses. Individually bound, the lecture "chapters" are printed as separate booklets and gathered into an attractively designed looseleaf binder. This format contributes to an orderly file of information for use as a working reference and a continuously updated addition to your personal library. It allows you to tailor it to your own ideas and needs by refiling, reclassifying, or supplementing the material with your own notes, reprints, or other material.

Published annually. Price per volume $15.00 (U.S.), $20.00 (elsewhere). Fourteen volumes are currently available.

PROBLEMS IN ANESTHESIA

A new quarterly series for general anesthesiologists and residents in anesthesia

NEW!

Robert R. Kirby, M.D., and
David L. Brown, M.D., Editors

Devoted to the daily questions and challenges familiar in the practice of every anesthesiologist: safety for high-risk patients, monitoring, cardiac considerations, OR emergencies, perioperative care. Original, invited articles are directed entirely to *clinical* problems; no research papers or reviews appear. Each volume offers ten to twenty articles, planned by the guest editor or editors and grouped around one or two central themes. Durable, hardbound volumes, generously illustrated, fully indexed, with no advertising, form a permanent and growing library for your permanent reference.

Published quarterly. Individual rate $55.00 (U.S.), $64.00 (elsewhere). Residents $35.00 (U.S. only).

PROBLEMS IN CRITICAL CARE

A new quarterly series for specialists in critical care

NEW!

Robert R. Kirby, M.D., and
Robert W. Taylor, M.D., Editors

Problems—patients with acute, life-threatening conditions—the raison d'etre of every critical care unit. Shock, trauma, drug overdose, cardiac emergencies, severe burns—the questions that are familiar in the daily practice of every anesthesiologist who serves as a member of the critical care team. Original, invited articles in this series are aimed foursquare at *clinical* questions, bringing you current information for better care of acutely ill patients. Each volume presents ten to twenty articles, planned by the guest editor or editors and centered around one or two specific topics. Durable hardbound volumes, fully illustrated and indexed, with no advertising, form a permanent resource that will prove its worth through the years.

Published quarterly. Individual rate $55.00 (U.S.), $64.00 (elsewhere). Residents $35.00 (U.S. only).

1792 **Lippincott**

J. B. Lippincott Company • *The Health Professions Publisher of Harper & Row, Inc.*
East Washington Square, P.O. Box 280, Philadelphia, PA 19105

Please enter my subscriptions to the publications checked:

- ☐ **Anesthesiology:** Individuals $30 (U.S.), $69 (elsewhere).*
- ☐ **Regional Anesthesia:** Individuals $37 (U.S.), $41 (elsewhere);* Residents $25 (U.S.)
- ☐ **ASA Refresher Courses in Anesthesiology:** Vol. 14 - $15 (U.S.), $20 (elsewhere)*
- ☐ **Problems in Anesthesia:** Individuals $55 (U.S.), $64 (elsewhere);* Residents $35 (U.S.)
- ☐ **Problems in Critical Care:** Individuals $55 (U.S.), $64 (elsewhere);* Residents $35 (U.S.)

*Except Japan.

☐ Please send information on previous volumes of the ASA Refresher Courses.

Prices quoted in U.S. funds for individuals only and subject to change.
Orders subject to the approval of Lippincott

Name ____________
Address ____________
City/State/Zip ____________

☐ Residents: To qualify for special rate, please indicate Hospital and Chief of Staff.
____

☐ Payment enclosed. ☐ Please bill me.
☐ Charge it: ☐ MasterCard ☐ VISA ☐ American Express
Card No. ____________ Expiration Date ____________
Signature ____________

A10596

Anaesthesia, 1987, Volume 42, pages 1037–1042

Courses in Anaesthesia

The information below is believed to be accurate but those intending to attend a course should check the details with the relevant organiser. Applications and further information cannot be proved by *Anaesthesia*.

FFARCS Part 1

DUNDEE			
Ninewells Hospital and Medical School, Dundee DD1 9SY	September 1987 to March 1988, Monday afternoons (followed by Part 2)	NO FEE	The Secretary, Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee DD1 9SY *Tel.* 0382 6011 *ext.* 2175
EDINBURGH			
Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW	Basic concepts in anaesthetic practice, 28 September to 2 October 1987, January 1988	FEE ON APPLICATION	University Secretary, Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW
Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW	Scientific basis of anaesthesia, 26–30 October, 1987, 25–29 April 1988	£150	Postgraduate Dean, Edinburgh Postgraduate Board for Medicine, Phizer Foundation, Hill Square, Edinburgh EH8 9DR *Tel.* 031 667 1010 *ext.* 4521
LONDON			
Department of Anaesthetics, St. Thomas' Hospital, London SE1 7EH	Day release, Fridays, 13 November 1987 to 29 January 1988	£120	Anaesthetic Course Secretary, Department of Anaesthetics, St. Thomas' Hospital, Lambeth Palace Road, London SE1 7EH
North London Hospitals' Course	10 September to 13 November 1987, 19 November 1987 to 28 January 1988, 6 March to 5 May 1988, 12 May to 14 July 1988	£250	Course Office, Room 107, Rayne Institute, University Street, London WC1E 6JJ *Tel.* 01 387 9300 *ext.* 5257
OXFORD			
Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford OX2 6HE	3-day course in May and November		Miss K. Bicknell, Administrative Assistant, Oxford Regional Committee for Postgraduate Medical Education and Training, The Medical School Offices, John Radcliffe Hospital, Headington, Oxford OX3 9DU

SHEFFIELD Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX	1 October to 10 December 1987 (Thursday mornings), 18–24 May 1988 (intensive course)		Dr C. S. Reilly, Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX *Tel.* 0742 766222 *ext.* 2510
WESSEX Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH	Intensive courses September 1987, January 1988, May 1988 (provisional dates)		Mrs Audrey High, Regional Postgraduate Administrator, Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH *Tel.* 0962 63511

FFARCS Part 2

DUNDEE Ninewells Hospital and Medical School, Dundee DD1 9SY	September 1987 to March 1988	NO FEE	The Secretary, Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee DD1 9SY *Tel.* 0382 6011 *ext.* 2175
EDINBURGH Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW	Scientific basis of anaesthesia 26–30 October 1987, 25–29 April 1988	£150	Postgraduate Dean, Edinburgh Postgraduate Board for Medicine, Phizer Foundation, Hill Square, Edinburgh EH8 9DR *Tel.* 031 667 1010 *ext.* 4521
LEEDS Leeds General Infirmary	September to July, alternate Wednesdays, 3 × 13-week terms	NO FEE FOR THOSE EMPLOYED IN REGION	The Department Secretary, Department of Anaesthesia, 24 Hyde Terrace, Leeds LS2 9LN *Tel.* 0532 431751 *ext.* 6172
LONDON Department of Anaesthetics, St Thomas' Hospital, London SE1 7EH	Day-Release, Fridays, 13 November 1987 to 15 April 1988	£120	Anaesthetic Course Secretary, Department of Anaesthetics, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH
MANCHESTER Manchester Medical School, Oxford Road, Manchester M13 9PT	One-week intensive course, 7–11 September 1987	£150	Secretary for Advanced Courses, Department of Postgraduate Medical Studies, Stopford Building, Oxford Road, Manchester M13 9PT

NEWCASTLE			
Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP	Day release, Wednesdays, 6 January 1988 to 22 June 1988	NO FEE	Secretary, University Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP *Tel.* 091 2619765 *or* 091 2325131 *ext* 24910
OXFORD			
Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford OX2 6HE	2-week residential course, February/March 1988		Miss K. Bicknell, Administrative Assistant, Oxford Regional Committee for Postgraduate Medical Education and Training, The Medical School Offices, John Radcliffe Hospital, Headington, Oxford OX3 9DU
SHEFFIELD			
Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX	1 October 1987 to 3 December 1987 (Thursday afternoons), 23–25 September 1987, 23–25 March 1988 (intensive courses)		Dr C. S. Reilly, Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX *Tel.* 0742 766222 *ext.* 2510
WESSEX			
Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH	Intensive course, March 1988 (provisional date)		Mrs Audrey High, Regional Postgraduate Administrator, Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH *Tel.* 0962 63511

FFARCS Part 3

BRISTOL			
Bi-Annual Intensive Course – Bristol Royal Infirmary, Bristol BS2 8HW	'The Bristol Crammer' 7–11 December 1987	£110	Dr L. E. Shutt, Department of Anaesthesia, Bristol Maternity Hospital, Southwell Street, Bristol BS2 8EG *Tel.* 0272 215411
Frenchay Hospital, Bristol BS16 1LE	9–13 May 1988		Dr J. A. Bennett, Department of Anaesthesia, Frenchay Hospital, Bristol BS16 1LE *Tel.* 0272 701212
CAMBRIDGE			
Addenbrooke's Hospital and Papworth Hospital	3-day intensive revision course, December 1987 and May 1988	£90	The Secretary, Anaesthetics Department, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ *Tel.* 245151 *ext.* 7432

DUNDEE			
Ninewells Hospital and Medical School, Dundee DD1 9SY	September 1987 to March 1988, Thursday afternoons	NO FEE	The Secretary, Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee DD1 9SY *Tel.* 0382 60111 *ext.* 2175
LEEDS			
St James' University Hospital, Leeds	September to July, alternate Wednesdays, 3 × 13-week terms	NO FEE FOR THOSE EMPLOYED IN REGION	The Departmental Secretary, Department of Anaesthesia, 24 Hyde Terrace, Leeds LS2 9LN *Tel.* 0532 431751 *ext.* 6172
LONDON			
Faculty of Anaesthetists, Royal College of Surgeons of England, London WC2A 3PN	3-week course, 11–29 April, 19 September to 7 October 1988	FEE ON APPLICATION	The Secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PN *Tel.* 01 405 3474
The East London Course	16 weeks, day release, Tuesdays, 8 September to 22 December 1987	£195	Course Secretary, Anaesthetics Unit, The London Hospital, Whitechapel, London E1 1BB *Tel.* 01 377 7725
Department of Anaesthetics, St Thomas' Hospital, London SE1 7EH	Day release, Wednesdays, 19 August to 30 December 1987	£180	Anaesthetic Course Secretary, Department of Anaesthetics, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH
MANCHESTER			
Manchester Royal Infirmary and Main Teaching Hospitals	2 one-week intensive courses, 16–20 November 1987, April 1988	FEE ON APPLICATION	Secretary for Advanced Courses, Department of Postgraduate Medical Studies, Stopford Building, Oxford Road, Manchester M13 9PT
NEWCASTLE			
Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP	Day release, Wednesdays, 6 January 1988 to 22 June 1988	NO FEE	Secretary, University Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP *Tel.* 091 2619765 or 091 2325131 *ext.* 24910
OXFORD			
Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford OX2 6HE	4-day course on clinical measurement, May and December		Miss K. Bicknell, Administrative Assistant, Oxford Regional Committee for Postgraduate Medical Education and Training, The Medical School Offices, John Radcliffe Hospital, Headington, Oxford OX3 9DU

SHEFFIELD			
Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX	16 October to 20 November 1987, 15 January 1988 to 18 March 1988 (Friday afternoons), 25–27 November 1987 (intensive course)		Dr C. R. Reilly, Department of Anaesthesia, The University of Sheffield, Beech Hill Road, Sheffield S10 2RX *Tel.* 0742 766222 *ext.* 2510
WESSEX			
Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH	Day-release course 7–14 December 1987, intensive course April 1988		Mrs Audrey High, Regional Postgraduate Administrator, Postgraduate Department, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester SO22 5DH *Tel.* 0962 63511

Other courses

BIRMINGHAM			
Postgraduate Medical Centre, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST	5–7 January 1988	FEE ON APPLICATION	Miss M. Wood, Postgraduate Medical Centre, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST
BRISTOL			
Frenchay Hospital, Bristol BS16 1LE	5-day course on Anaesthesia for developing countries and difficult locations, 30 November to 4 December 1987	£145	Dr J. A. Carter, Department of Anaesthesia, Frenchay Hospital, Bristol BS16 1LE
Royal Infirmary, Frenchay and Southmead Hospitals	Half-day release (Friday afternoons), teaching shared between hospitals		The Secretary, Department of Anaesthesia, Bristol Royal Infirmary, Bristol BS2 8HW *Tel.* 0272 230000
CARDIFF			
Department of Anaesthetics, University Hospital of Wales, Cardiff CF4 4XW	Organising clinical research, 22–23 October 1988		Mrs M. Thomas, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW
Department of Anaesthetics, University Hospital of Wales, Cardiff CF4 4XW	Intensive care course, 23–24 September		Dr J. M. Foy, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW

CARSHALTON			
Queen Mary's Hospital for Children, Carshalton, Surrey SM5 4NR	Paediatric anaesthesia, 3½ days, 16–19 February, 10–13 May, 11–13 October, 6–9 December 1988	£100	The Secretary, Postgraduate Medical Centre, Queen Mary's Hospital for Children, Carshalton, Surrey SM5 4NR *Tel.* 01 643 3300
EDINBURGH			
Phizer Foundation, Hill Square, Edinburgh EH8 9DR	Local anaesthesia, 1–2 October, 1987 6–7 October 1988	FEE ON APPLICATION	Postgraduate Dean, Edinburgh Postgraduate Board for Medicine, Phizer Foundation, Hill Square, Edinburgh EH8 9DR *Tel.* 031 667 1010 *ext.* 4521
LEEDS			
University Department of Anaesthesia, 24 Hyde Terrace, Leeds LS2 9LN	One-week full-time course of practical demonstrations on clinical measurement, 4–8 January 1988	NO FEE FOR THOSE EMPLOYED IN REGION	The Departmental Secretary, Department of Anaesthesia, 24 Hyde Terrace, Leeds LS2 9LN *Tel.* 0532 431 751 *ext.* 6172
LONDON			
Institute of Dental Surgery, Eastman Dental Hospital, 256 Gray's Inn Road, London WC1X 8LD	General anaesthesia and sedation, 9–13 November 1987, optional 1–3 weeks practical course available	1 week £140, 2 weeks £160, 3 weeks £180, 4 weeks £200	The Course Administrator, Institute of Dental Surgery, Gray's Inn Road, London WC1X 8LD *Tel.* 01 837 3646 *ext.* 2044
Faculty of Anaesthetists, Royal College of Surgeons of England, London WC2A 3PN	One-week refresher course, 13–17 June 1988	FEE ON APPLICATION	The Secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, London WC2A 3PN 35–43 Lincoln's Inn Fields, London WC2A 3PN *Tel.* 01 405 3474
OXFORD			
Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford OX2 6HE	One-week residential course, Current trends in pain relief, September		Miss K. Bicknell, Administrative Assistant, Oxford Regional Committee for Postgraduate Medical Education and Training, The Medical School Offices, John Radcliffe Hospital, Headington, Oxford OX3 9DU

Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
Richard J. Kitz, Emanuel M. Papper, John J. Bonica,
Werner Flacke and A.H. Giesecke, Jr.

Publication: Quarterly
Subscription: Volume 6, 1987
Institutions: £56.00 (UK)/$75.00 (Overseas)

Seminars in Anesthesia will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

From a recent issue

Anesthesia Disasters: Incidence, Causes, and Preventability, *R. L. Keenan*

Oxygen Monitoring in the Operating Room, *J. B. Brodsky*

Oximetry as a Warning of Inadequate Ventilation, *D. A. Paulus*

Capnometry and Capnography: The Anesthesia Disaster Early Warning System, *D. B. Swedlow*

Respiratory Monitoring to Detect and Avoid Anesthetic Disasters: Mass Spectrometry, *M. Lichtiger*

Monitoring of Anesthetic Halocarbons: Self-Contained ('Stand-Alone') Equipment, *C. Whitcher*

Development Directions for Monitoring in Anesthesia, *C. K. Waterson and J. M. Calkins*

The Standard of Care and Where It Comes From, *D. S. Rubsamen*

Coupon

Seminars in Anesthesia

To: Journals Marketing Department
Academic Press Inc. (London) Ltd
24-28 Oval Road
London NW1 7DX, England

Please tick

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.. Name (Capitals) ....

Address ....

.... Date..........................

European Journal of Anaesthesiology

Journal Editor
M.D. Vickers *Cardiff*

Deputy Editor
P. Foëx *Oxford*

Editor of Commissioned Articles
C. Prys-Roberts *Bristol*

Assistant Editors
J.M. Desmonts *Paris*
T.E.J. Healy *Manchester*
W.R. MacRae *Edinburgh*
J. Tarnow *Berlin*
J. Viby *Mogensen*

Advisory Editorial Board
H. Bergmann *Linz*
J.B. Brückner *Berlin*
S. Couremenos *Athens*
J.F. Crul *Nijmegen*
J.M. Desmonts *Paris*
W. Dick *Mainz*
W. Jurczyk *Poznan*
J. Lassner *Paris*
C. Manni *Rome*
M.A. Nalda-Felipe *Barcelona*
O. Norlander *Stockholm*
J.C. Otteni *Strasbourg*
C. Prys-Roberts *Bristol*
M. Rosen *Cardiff*
K. Steinbereithner *Vienna*
M.K. Sykes *Oxford*
T. Tammisto *Helsinki*
M.D. Vickers *Cardiff*
K.H. Weis *Würzburg*
J.S.M. Zorab *Bristol*

The *European Journal of Anaesthesiology*, the official publication of the European Academy of Anaesthesiology, publishes original work of high scientific quality. Preference is given to experimental work or clinical observation in man, and to laboratory work of clinical relevance. Each issue contains a commissioned review by an authority in a field of interest to those working in anaesthesiology or intensive care. Abstracts of Academy meetings, editorials, book reviews, news and notices are also included.

Subscription Information
European Journal of Anaesthesiology is published bi-monthly. Subscription rates for 1987 are £60.00 (UK and overseas), $99.50 (Japan). Subscription details for North America are available from Year Book Medical Publishers, 35 East Wacker Drive, Chicago, Illinois 60601, USA.

Order Form

Please tick the appropriate box and return to **Blackwell Scientific Publications Ltd, P.O. Box 88, Oxford, England.**

☐ I would like to subscribe to *European Journal of Anaesthesiology*

☐ I wish to pay by cheque/money order *(delete as necessary)* and enclose the sum of ....

☐ I wish to pay by Access/Barclaycard/VISA/Mastercard *(delete as necessary)*

Please debit my credit card no. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Expiry date........................... with the sum of ....

Signature... Date. ....

☐ Please send me a specimen copy of *European Journal of Anaesthesiology*

Name ....

Address ....

....

Blackwell Scientific Publications
P.O. Box 88, Oxford, England

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

Overseas and Associate Membership

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

Junior Membership (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation on the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

Membership Fees (inclusive of the journal *Anaesthesia*)

Ordinary Members: Subscription **£65** (Husband and wife **£50** each)

Overseas and Associate Members: Subscription **£65**

Junior Members: Subsciption **£38** (**£50** after 3 years if still in training)

Retired Members: who receive *Anaesthesia* **£10** (there is no subscription for those who do not).

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.)

........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate
BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

....

(Signed)..

Address..
....Hospital Tel. No:.......................................
....Home Tel. No:..

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)...
(NAME IN BLOCK LETTERS)
Address..
BLOCK LETTERS

2. (Signed)...
(NAME IN BLOCK LETTERS)
Address..
BLOCK LETTERS

* See the reverse of this page for details of membership categories.
† One sponsor must be an Ordinary Member of the Assocation.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (UK).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence are to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s), degrees and designations should be typed in lower case below the line. Initials should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction*, *Methods*, *Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left-hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

Use the form of reference adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscripts submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

Roueche B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the left-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS, ABBREVIATIONS AND STATISTICS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Systéme International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia*, *Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 42, no. 9, September 1987

EDITORIAL

Down the tube
R. Greenbaum 927

ORIGINAL ARTICLES

Propofol infusion for sedation in intensive care
L.H. Newman, J.C. McDonald, P.G.M. Wallace and I. McA. Ledingham 929
One lung anaesthesia. Cardiovascular and respiratory function compared during conventional ventilation and high frequency jet ventilation
J. Jenkins, E.W.J. Cameron, A.C. Milne and R.M. Hunter 938
The effects of vecuronium on intra-ocular pressure
R.K. Mirakhur, W.F.I. Shepherd, G.G. Lavery and P. Elliott 944
Suxamethonium in myasthenia gravis
A.P. Wainwright and P.M. Brodrick 950
Intercostal catheterisation. An alternative approach to the paravertebral space
A. Mowbray, K.K.S. Wong and J.M. Murray 958

CASE REPORTS

A red patient: immunological reaction to glycine?
P.E. Moskovits, P. Riches and N. Soni 962
Removal of a giant ovarian cyst. Anaesthetic and intensive care management
P. Morrison and G. Morgan 965
Combined unilateral high frequency jet ventilation and contralateral intermittent positive pressure ventilation
B.A. Morgan, D. Perks, I.D. Conacher and M.L. Paes 975
Ketamine infusion. Its use as a sedative, inotrope and bronchodilator in a critically ill patient
G.R. Park, A.R. Manara, L. Mendel and P.E. Bateman 980
Upper limb sympathetic blockade following intercostal nerve blocks
G. Purcell-Jones, H.M. Speedy and D.M. Justins 984
Persistent pneumothorax treated with continuous positive airway pressure
M.G. Elphinstone and I.S. Grant 987
Carcinoid syndrome and intravenous cyproheptadine
G. Solares, E. Blanco, S. Pulgar, C. Diago and F. Ramos 989
Recurarisation after vecuronium in a patient with renal failure
M.W. Cody and F.M. Dormon 993

HISTORICAL NOTE

Brünings' bronchoscopic mask
H.A. Condon 996

SPECIAL ARTICLE

The new generation gelatins. A review of their history, manufacture and properties
J.M. Saddler and P.J. Horsey 998

FORUM

The morphine sparing effects of diclofenac sodium following abdominal surgery
N.B.A. Hodsman, J. Burns, A. Blyth, G.N.C. Kenny, C.S. McArdle and H. Rotman 1005
The control of intra-ocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique
M.A. Abbott and J.R. Samuel 1008
Tracheal tubes in neuroanaesthesia. Nylon reinforced latex rubber tracheal tubes
P.J. Wright and J.V.B. Mundy 1012

CORRESPONDENCE 1015

BOOK REVIEWS 1026

ANAESTHETIC LITERATURE 1029

COURSES IN ANAESTHESIA 1037

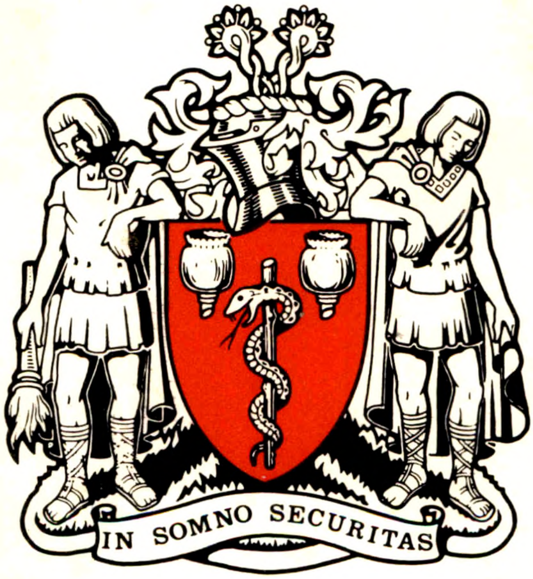
Printed in Great Britain by Richard Clay Ltd, Bungay, Suffolk

Acc.
15.12.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 42 Number 10 October 1987



Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London San Diego New York Berkeley Boston
Sydney Tokyo Toronto

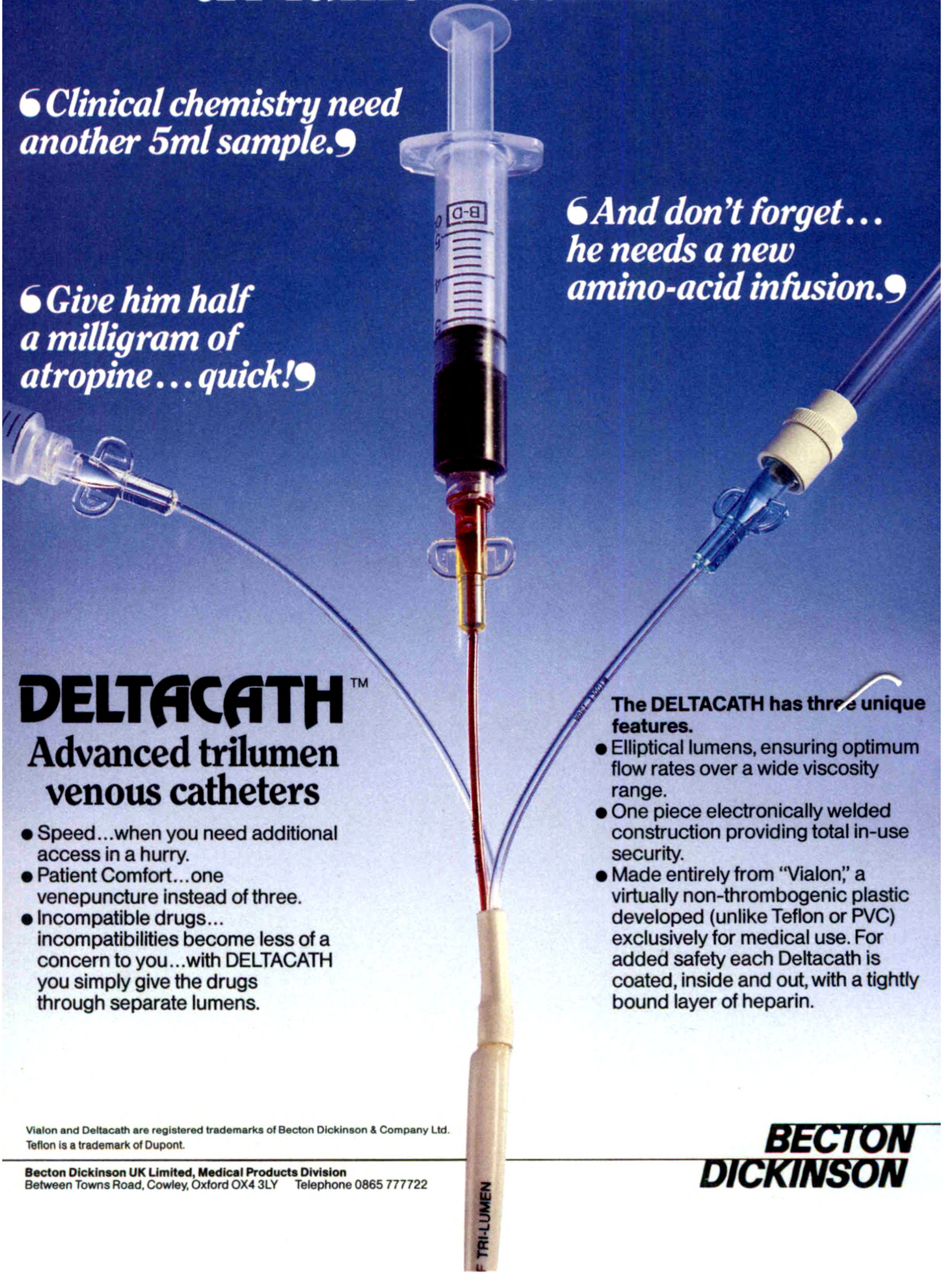
ISSN 0003-2409

When would I ever need to use a tri-lumen catheter?

‘Clinical chemistry need another 5ml sample.’

‘Give him half a milligram of atropine…quick!’

‘And don’t forget… he needs a new amino-acid infusion.’



DELTACATH™

Advanced trilumen venous catheters

- Speed…when you need additional access in a hurry.
- Patient Comfort…one venepuncture instead of three.
- Incompatible drugs… incompatibilities become less of a concern to you…with DELTACATH you simply give the drugs through separate lumens.

The DELTACATH has three unique features.

- Elliptical lumens, ensuring optimum flow rates over a wide viscosity range.
- One piece electronically welded construction providing total in-use security.
- Made entirely from “Vialon,” a virtually non-thrombogenic plastic developed (unlike Teflon or PVC) exclusively for medical use. For added safety each Deltacath is coated, inside and out, with a tightly bound layer of heparin.

Vialon and Deltacath are registered trademarks of Becton Dickinson & Company Ltd.
Teflon is a trademark of Dupont.

Becton Dickinson UK Limited, Medical Products Division
Between Towns Road, Cowley, Oxford OX4 3LY Telephone 0865 777722

BECTON DICKINSON

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

---

Editor J. N. LUNN
Assistant Editors M. MORGAN, R. GREENBAUM, R. M. JONES, A. R. AITKENHEAD
Editor of *Anaesthesia News* J. N. HORTON
Editorial Board
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
Ex officio
The President of the Association M. ROSEN
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association P. MORRIS
The Immediate Past Honorary Secretary of the Association M. T. INMAN

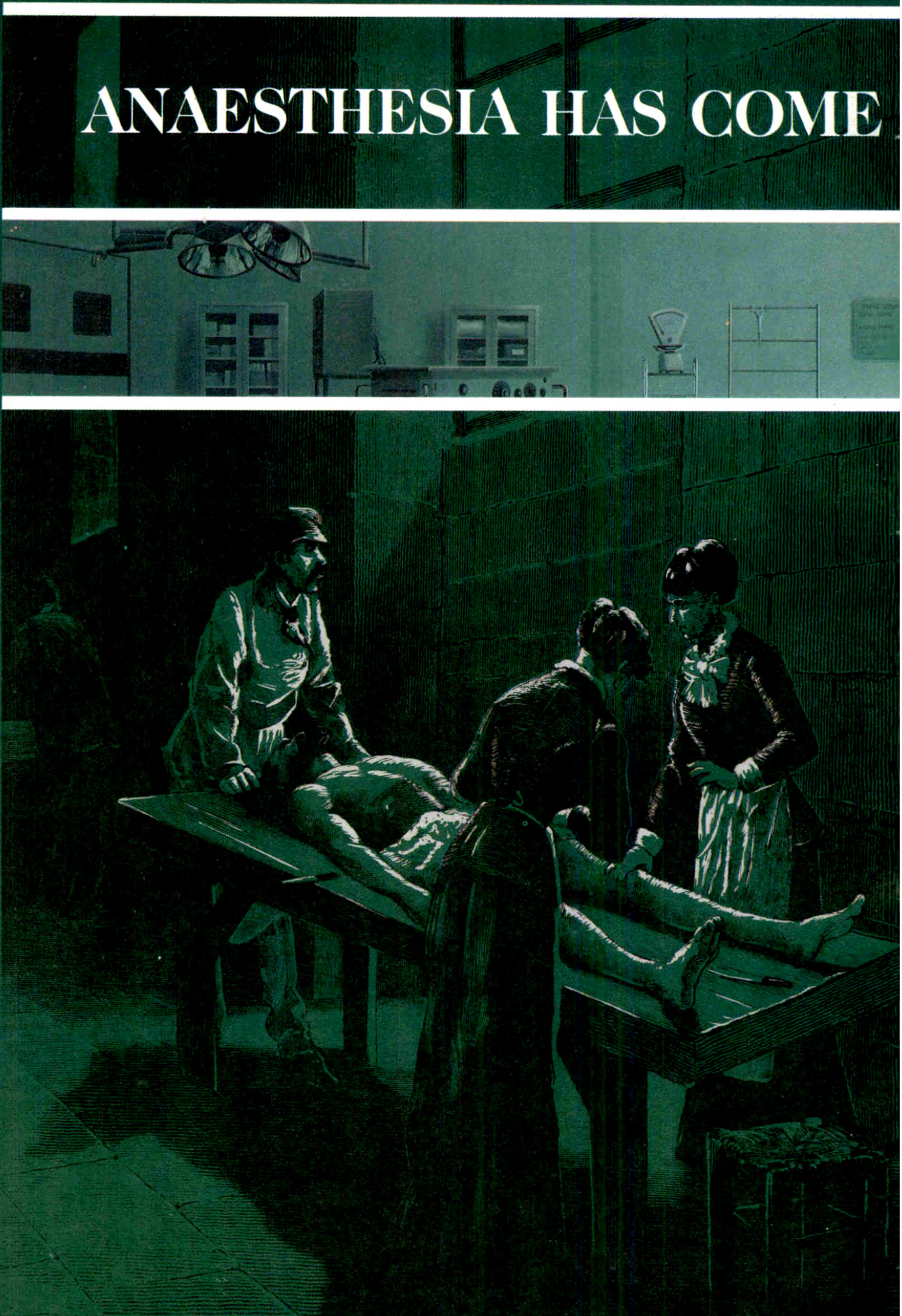
Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.

Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. A written statement of this acceptance may be requested by the Editor.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Limited for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
1987, Volume 42, 12 issues. Inland £90.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300–0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
U.S. POSTMASTER: send address changes to "Anaesthesia", c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Second class postage paid at Jamaica, New York 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
© 1987 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.
ISSN 0003–2409



PRESCRIBING INFORMATION

Ingredients: *Each 1 ml contains:* Glycopyrrolate USP 500 micrograms (0.5mg), Neostigmine Methylsulphate 2500 micrograms (2.5mg). **Indication:** Reversal of residual non-depolarising (competitive) neuromuscular block. **Dosage and Administration:** *Intravenous injection.* Adults and Older Patients: 1-2ml (2500 micrograms neostigmine methylsulphate/500 micrograms glycopyrrolate to 5000 micrograms neostigmine methylsulphate/1000 micrograms glycopyrrolate) over a period of 10-30 seconds. Alternatively 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. *Children:* 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. These doses may be repeated if adequate reversal is not achieved. Total doses in excess of 2ml are not recommended. **Contra-indications:** Hypersensitivity to ingredients. Mechanical obstruction of gastrointestinal or urinary
tracts. Concomitant administration of suxamethonium. **Side Effects:** Neo
induced (muscarinic) side effects — bradycardia, increased oropharynge
tions, cardiac dysrhythmias, bronchospasm, increased gastrointestinal
etc. Glycopyrrolate induced side effects — dry mouth, difficulty in mic
cardiac dysrhythmias, disturbances of visual accommodation, inhibition o
ing. **Precautions:** Use with caution in patients with bronchospasm,
bradycardia, fever, glaucoma, coronary artery disease, congestive hear

A.H.ROBINS

ONG WAY…

...SO HAS REVERSAL

In recent years, many advances have been made in the field of anaesthesia, including reversal of residual neuromuscular blockade.

A. H. Robins has been a major contributor to this area with Robinul, an anticholinergic agent which provides significant advantages over atropine.

Robinul produces less initial tachycardia, and better protection against the peripheral muscarinic effects of neostigmine than atropine. In addition, the quality of recovery after Robinul is better than after atropine, due to limited penetration of Robinul into the central nervous system.

Clinical experience has demonstrated that simultaneous administration of Robinul and neostigmine is associated with greater cardiostability at reversal, than separate injections. This had led A. H. Robins to develop ROBINUL-NEOSTIGMINE injection, a ready prepared mixture containing standard doses of Robinul and neostigmine for reversal, in a 1ml ampoule.

Robinul-neostigmine injection provides dependable and convenient reversal of residual neuromuscular blockade, contributing further towards improvements in anaesthesia.

srhythmias, hypertension, thyrotoxicosis, epilepsy or Parkinsonism.
aution in patients with intestinal anastomoses. Safety in pregnancy/
as not been established. **Basic NHS price** £9.40 (10 x 1ml ampoules).
egory POM **Package Quantities** Packs of 10 ampoules. **Further**
on Robinul Neostigmine Injection can be used when atropine has been
pre-operative anti-cholinergic. **Product Licence Number** 0100/0099.
uthorisation Number 86/27/1

ROBINUL®
GLYCOPYRROLATE
NEOSTIGMINE

Wellcome

International symposium on recent developments in muscle relaxation

at The Royal College of Surgeons of England London WC2
Saturday November 28th, 1987. Registration at 9.30am.

For further information and programme contact Conference Secretariat,
c/o 4 Nicholas Road, Hunters Ride, Henley-on-Thames, Oxon.

LEICESTER DEPARTMENT OF ANAESTHESIA

FFARCS EXAMINATION (Part 3)

REVISION COURSE

A whole time course of lectures and tutorials

25 April–29 April 1988

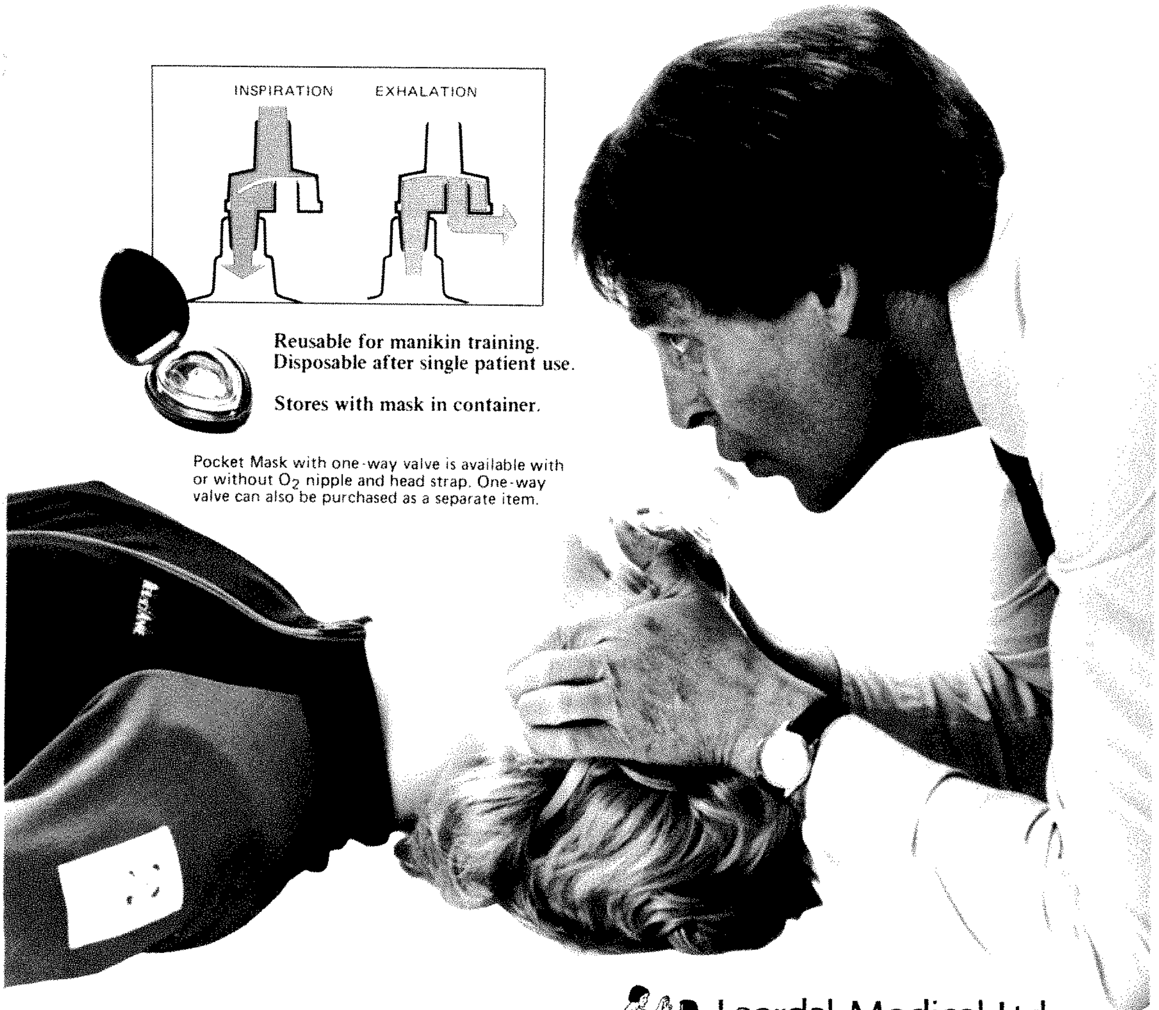
FEE £35 (except doctors employed in the Trent Region)

Further Information:
The Secretary: Department of Anaesthesia, The Leicester Royal Infirmary,
Leicester, LE1 5WW. Tel: 0533 541414 Ext 474

Other courses in Anaesthesia for the FFARCS Examination:
Part 1 Whole time lecture course 18–22 January 1988
Part 2 Half-day Friday afternoons 9 October 1987–22 April 1988
Part 3 Clinical measurement Friday afternoons 21 August–2 October 1987

Further information from
the Department of Anaesthesia, The Leicester Royal Infirmary

Laerdal Pocket Mask
with new One-Way Valve
Diverts patient's exhalation away from the rescuer



Reusable for manikin training.
Disposable after single patient use.

Stores with mask in container.

Pocket Mask with one-way valve is available with or without O_2 nipple and head strap. One-way valve can also be purchased as a separate item.

Laerdal Medical Ltd.
Laerdal House, Goodmead Road, Orpington, Kent BR6 OHX
Tel. Orpington (0689) 76634. Telex 8955251 LML G

WORKSHOP ON EMERGENCIES IN OBSTETRICS AND OBSTETRIC ANAESTHESIA

December 11th and 12th 1987
University Hospital of Wales, Cardiff

Guest Speaker: Dr. Rosemary MacDonald, St. James Hospital, Leeds.
Other Speakers Include: Professor M. Rosen
Professor B. Hibbard
Dr. G. A. D. Rees
Dr. M. Harmer

COST: **£120**

Details may be obtained from:
Dr. M. Harmer, Consultant Anaesthetist, Department of Anaesthetics,
University Hospital of Wales, Heath Park, Heath, Cardiff, CF4 4XW

Closing Date for Applications: **27th November 1987**

NORTH EAST THAMES REGIONAL HEALTH AUTHORITY
OAKLEA REGIONAL TRAINING CENTRE, BUCKHURST HILL, ESSEX

Basic Anaesthesia

NEW F.F.A.R.C.S. PART I COURSE (RESIDENTIAL)
25th–30th JANUARY 1988 – Tuition Fee: £175.00
Closing Date: 15th January 1988

Revision Course for those with over six months in Anaesthesia
Evening Tutorial Work
Emphasis is on clinical sessions, mock examinations, lectures by distinguished visiting lecturers
Fullboard (£30.00 per day)
Approved for Study Leave under HM(67)27

Application forms and details from:
MRS. P. BLUMSOM – Oaklea Regional Training Centre
Telephone Enquiries 01–504 0061

COURSE ORGANISER: **Dr. W. D. J. Cantrell F.F.A.R.C.S.**
Consultant Anaesthetist, Whipps Cross Hospital

New Journal for 1987 . . .

JOURNAL OF CARDIOTHORACIC ANESTHESIA

Editor-in-Chief **Joel A. Kaplan**

Associate Editors
J. Earl Wynands, Cardiac Anesthesia
Roger Wilson, Thoracic Anesthesia
Dennis T. Mangano, Vascular Anesthesia

The Journal of Cardiothoracic Anesthesia is primarily aimed at anesthesiologists dealing with patients undergoing cardiac, thoracic, or vascular surgical procedures. In addition, a multidisciplinary approach will include contributions from cardiac, vascular, and thoracic surgeons, cardiologists, and other internists, intensivists, and related basic scientists. Emphasis will be placed on rapid publication of clinically relevant material applicable to the perioperative period. The purpose of the journal is to consolidate and disseminate original information in these important subspecialties of anesthesiology.

The Journal will publish editorials, original articles, brief clinical studies, large clinical series, case reports, invited state-of-the-art review articles, invited reviews of new drugs and equipment, controversial issues, pertinent abstracts from other journals, letters to the Editor, meeting summaries, news and notes, and book reviews. Innovative submissions using the latest techniques (e.g., two-dimensional color flow doppler and/or computer graphics) will be published at the Journal's expense. In addition, special supplement issues will highlight important topics. The Journal will be international in scope, with submissions encouraged from all continents. Every effort will be made to publish important new information in the shortest possible time. To further this goal of rapid publication in these constantly changing subspecialties, authors will be able to request an "expedited review" of their submissions. A positive "expedited review" will lead to rapid publication for new and controversial material.

Publication: Bi-monthly
Subscription: Volume 1, 1987
Full Rate: $109.00 Overseas / £84.00 (U.K. Only)

For full subscription information and sample copies please apply to Journals Marketing Department at the addresses below.

Grune & Stratton

24–28 OVAL ROAD, LONDON NW1 7DX, UK
ORLANDO, FLORIDA 32887, USA

VYGON

Many speak of Seldinger but . . .

VYGON
124
leader cath
Made in France
Cathéter intravasculaire ORX avec guide métallique (méthode de Seldinger) pour la voie sous-clavière
XRO intravascular catheter with metal spring guide (Seldinger-method) for subclavian introduction
VYGON

Seldinger speaks only of Leader-Cath

S-I Seldinger

Sven-Ivar Seldinger

Vygon (UK) Limited, Bridge Road,
CIRENCESTER, Glos., GL7 1PT.
Telephone: (0285) 67051 Telex: 43342 VYGON G

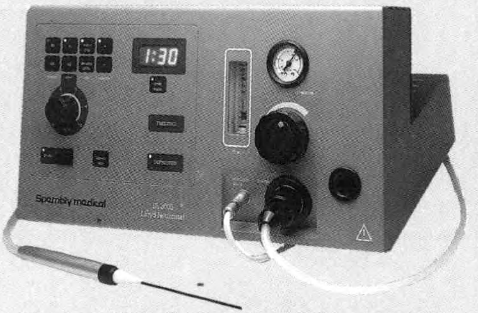
"Please send me details of the Leader-Cath range"

Name:
Designation:
Hospital: Ext:
Address:
Telephone:

Pain management in hospital and the home

Spembly Medical is foremost in the discipline of Pain Management. The Company has earned a unique reputation for its development of high quality instrumentation, particularly for the techniques of Cryoanalgesia and TENS.

An excellent example is the SL2000 Lloyd Neurostat. It adds a new perspective to the management of both acute and chronic pain via localised freezing of nerves. Treatment by Cryoanalgesia is of particular benefit for relieving post-operative pain and in conditions such as facet rhizolysis, coccydynia and neuroma formation.



Equally, the Spembly Medical 140 Cryounit, used in conjunction with the Maiwand probe, is an established method of freezing the intercostal nerves prior to closing the thorax — a recognised means of providing post-thoracotomy pain relief.

Obtaining pain relief, without recourse to drugs, through treatment by TENS is rapidly increasing. Outstanding for this technique is the Pulsar range — a family of small, lightweight battery operated units which enable more patients to obtain greater benefits from TENS over a wider range of clinical conditions. Significantly, Spembly Medical is the first to have designed a special unit for use in Obstetrics.

Spembly medical

Spembly Medical Limited
Newbury Road, Andover, Hampshire,
SP10 4DR, England
Telephone: (0264) 65741 Telex: 47403

Spembly Medical Pain Management products are UK manufactured.

Please clip and return this coupon to Spembly Medical Limited,
Newbury Road, Andover, Hampshire, SP10 4DR, England, for more details on:— GP/A/09

☐ SL2000 Lloyd Neurostat ☐ 140 Cryounit ☐ TENS Pulsar ☐ Obstetric Pulsar

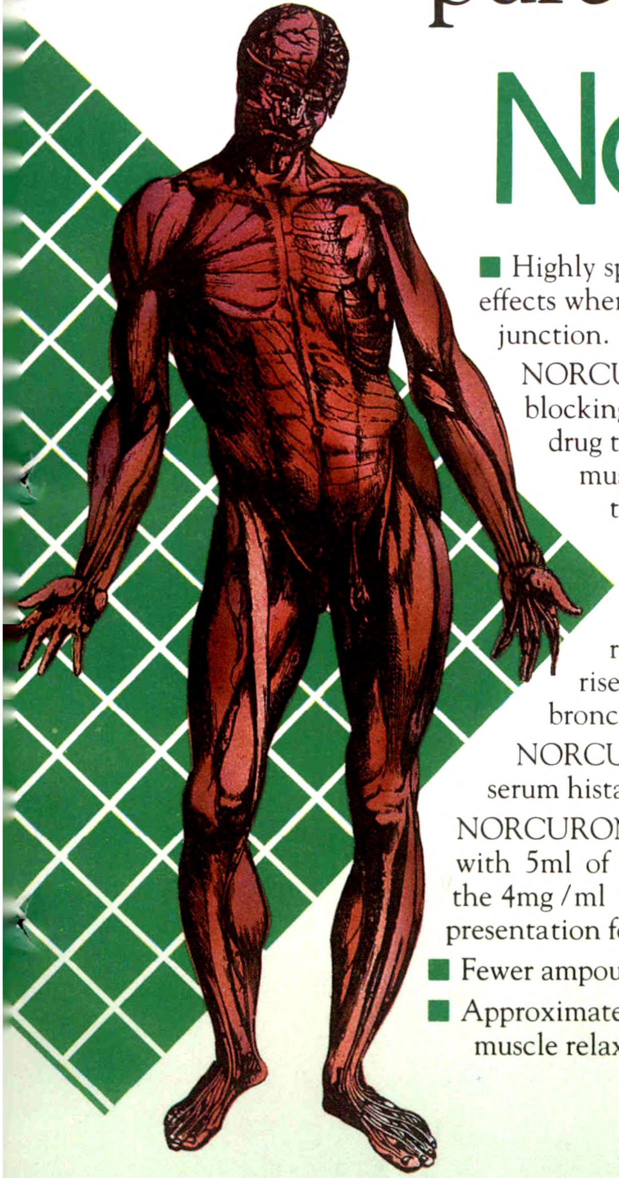
NAME ________ POSITION ________

ADDRESS ________

____

________ TELEPHONE ________

Muscle relaxation, pure and simple



NORCURON®

vecuronium bromide

- Highly specific – Muscle relaxants cause cardiovascular effects when their action is not specific for the neuromuscular junction.

NORCURON ". . . is the most specific neuromuscular blocking agent that has ever been synthesized. It is the drug that has by far the fewest side effects of any neuromuscular blocker. As a result it has the highest therapeutic ratio . . . A dose can be selected that will give either short or long term duration of action."[1]

- Histamine release unlikely – Some muscle relaxants cause histamine release. This may give rise to such side effects as hypotension and bronchospasm.

NORCURON ". . . at 3.5 times the ED_{95} does not alter serum histamine levels."[2]

NORCURON is now available in a 10mg injection top vial with 5ml of water for injection as solvent. This replaces the 4mg / ml ampoule, the result being a more convenient presentation for the anaesthetist.

- Fewer ampoules to open.
- Approximately equipotent volume for volume with other muscle relaxants i.e. Pavulon.

NORCURON

Muscle relaxation,
pure and simple

10mg/vial presentation

Organon Teknika Limited
Cambridge Science Park, Milton Road,
Cambridge CB4 4FL

---

1. Feldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
2. Basta SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 183-184

Prescribing Information: Norcuron vials of 10mg vecuronium bromide with 5ml ampoule water for injection. **Uses:** non-depolarising neuromuscular blocking agent of short to medium duration. **Dosage:** Intravenous initial 0.0 to 0.10mg/kg incremental 0.03 to 0.05mg/kg. **Contraindications:** none known. Since there is no experience with the use of Norcuron in pregnant women, it cannot be recommended during pregnancy. Clinical studies show tha Norcuron can be used in childbirth by Caesarian section without effect on the newly born child. **Precautions and warnings:** In renal insufficiency a slight prolongation of neuromuscular block can be expected. Use very smal doses, and extreme caution in myasthenia gravis or myasthenic syndrome unless prolonged post-operative respiratory assistance is intended. Dose carefully in myopathy, severe obesity, electrolyte disturbances, altered pH and afte poliomyelitis or dehydration. Neuromuscular blockade can be reversed with adequate doses of neostigmine together with atropine. **Interaction:** it is dangerous to give depolarising drugs (e.g. suxamethonium chloride) following non-depolarising drug (e.g. Norcuron). Alkylating drugs (nitrogen mustards) may be a hazard in anaesthesia involving muscle relaxants. Anaesthetics, other drugs and the condition of the patient, may affect the magnitude an or duration of action of **Norcuron** – see Data Sheet. **Side-effects:** none during clinical testing. **Overdosage:** use standard reversal agents, e.g. neostigmine or pyridostigmine. **Packs:** 20 vials 10mg **Norcuron,** 20 ampoules 5ml wate for injection. PL: 3524/0013.

Prescribing Information: FORANE® (isoflurane) **Indications:** for inhalation anaesthesia. **Dose:** induction should begin at 0.5% and be adjusted appropriately. Maintenance concentrations generally lie between 1.0% and 2.5%. Elderly: lesser concentrations normally required. Children: adequate data are not available in children under two years of age. **Contraindications:** know sensitivity to Forane, or a history of malignant hyperthermia following a previous adminstration. **Side-effects:** hypotension and respiratory depression. Shivering, nausea and vomiting may occur during recovery. **Basic N.H.S. price:** £33.50 per 100ml. **P.L. Number:** 0037/0115.

Abbott Laboratories Limite
Queenborough, Kent ME11 5E

Anaesthesia, 1987, Volume 42, pages 1043–1044

Editorial

Future organisation of anaesthetic health care

'It was as true,' said Mr Barkis, 'as taxes is. And nothing is truer than these.' Charles Dickens.

Dissatisfaction with the National Health Service was a major issue in the last election in the United Kingdom, although not sufficiently felt so as to sway the outcome. It is clear that some patients, doctors, nurses and other professional groups perceived the service to be unsatisfactory despite greatly increased public expenditure, and this is probably true for other countries' medical services.

The basic problems for anaesthetists in the United Kingdom are concerned with an inability to practice satisfactorily, and not with salary, although by Western standards that is not high. Lists cancelled at short notice and poor utilisation of theatre time are frustrating and time wasting, not to say uneconomic. Of the many reasons for these disruptions some should be soluble: better communications between surgeons and anaesthetists could save many lists. It would be a move forward if each 'miss' was analysed formally by a theatre panel. Lack of trained assistance for the anaesthetist is an ever-present problem and causes lists to be postponed. Recently a Working Party of the Association of Anaesthetists of Great Britain and Ireland, noted that a staffing level of one assistant per theatre, which is the establishment in many Health Districts, is inadequate for cover for illness and holidays and leads to daily difficulty with meal breaks. There is an intrinsic conflict between clearing up after the previous operation and being available in the anaesthetic room for the next induction of anaesthesia. It would be an essential step in improving efficiency, throughput and harmony, therefore, to increase staffing levels of assistants.

In addition, there is a recurrent, unsettled debate about who should undertake these assistant duties for the anaesthetist. It is surely time to reconsider present training schemes, since the Lewin proposals seem no longer appropriate to modern developments. The role of the trained nurse in assisting the anaesthetist varies widely and has not yet been defined satisfactorily. All these issues must be addressed by the Association if we are to improve anaesthetic services.

Lack of nurses outside the operating theatres is now a constricting factor in determining the quality of anaesthetic work, particularly in the intensive care unit and for postoperative care. It is unlikely, however, that there will ever be sufficient nurses available for the way in which hospitals are organised at present, whatever financial schemes are devised. There are problems with recruitment of nurses even in countries with very different salary structures (which includes even the United States of America and the Soviet Union). This thus appears to be an international problem in which there are now more opportunities for potential nursing recruits in society and there are falling birth rates. Anaesthetists should therefore encourage the optimum use of nursing skills necessary now to advances in our specialty, with the implementation of progressive patient care leading to the concentration of nursing and other facilities in sufficient recovery, high dependency or step down units and intensive care beds. Few or no nurses would be required elsewhere in the hospital.

Anaesthesia is essentially low risk but surgery is commonplace, so anaesthetic errors can lead to many deaths. Every year in the United Kingdom and probably elsewhere in the world, more deaths result completely or partly from errors of anaesthesia[1] than from AIDS, which is not a statistic which anaesthetists can view with equanimity. Anaesthetists must work harder to eliminate each element of preventable causes. We must concentrate particularly on improvements in practice and training, and then on the introduction of safer equipment and better monitoring devices which are now available and urgently necessary.

There appears at present to be a determination by Government to improve the Health Service and public satisfaction with it. The Association can play an important part by encouraging wide discussion

0003–2409/87/101043 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

to search for new ideas, and by examining possible new ways to provide better anaesthetic health care. When these are identified we should encourage local experiment to test each proposal thoroughly before national adoption. It is always safer to build from experience to ensure value for the taxes we all pay.

Association of Anaesthetists
of Great Britain and Ireland,
9 Bedford Square,
London WC1B 3RA

M. ROSEN
President

Reference

1. LUNN JN, MUSHIN WW. *Mortality associated with anaesthesia.* Nuffield Provincial Hospitals Trust, 1982.

Editorial notices

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 3 months of receipt.

Submission of Manuscript

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1:** 432–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1987, Volume 42, pages 1045–1050

Anaesthetic properties of pregnanolone emulsion

A comparison with alphaxolone/alphadolone, propofol, thiopentone and midazolam in a rat model

S. HØGSKILDE, J. WAGNER, P. CARL AND M. BREDGAARD SØRENSEN

Summary

The anaesthetic properties of pregnanolone emulsion, a new steroid preparation for intravenous administration, were evaluated in rats and compared to those of Althesin, propofol, thiopentone and midazolam. The therapeutic index was found to be 50% higher than that of Althesin and 6–8 times higher than those of propofol, thiopentone and midazolam. Induction with pregnanolone emulsion was reliable and fast, with only minor excitatory side effects, although induction time was longer compared to Althesin, propofol and thiopentone. Movement of unstimulated rats during sleep was similar to that seen with Althesin but movement on painful stimulation was less than with propofol and thiopentone. Recovery was rapid and smooth, and the proportion of sleeping time to recovery time was higher than found for the other four anaesthetics. No cumulative effects were seen on repeated administration and there were no venous sequelae. The results indicate that pregnanolone emulsion may provide a short-acting, less cumulative and less toxic alternative to existing intravenous anaesthetic agents.

Key words

Anaesthetics, intravenous; pregnanolone, Althesin, propofol, thiopentone.
Hypnotics, benzodiazepines; midazolam.

Althesin, a mixture of the two 5α reduced progesterone derivatives, alphaxolone and alphadolone, appeared to have many of the properties of the ideal intravenous anaesthetic.[1,2] However, a high incidence of hypersensitivity reactions terminated its clinical use. The solubilising agent Cremophor EL was suspected as the causative agent even though a contribution of the steroids could not be excluded.[3]

Pregnanolone emulsion is a new steroid preparation for intravenous administration, with anaesthetic properties comparable to those of Althesin.[4] The preparation differs from Althesin in several ways. The active ingredient, pregnanolone, is a 5β reduced metabolite of progesterone, a naturally occurring steroid,[5] and the preparation does not contain Cremophor EL. It is solubilised in soya bean oil and emulsified in a similar way to diazepam in the form of Diazemuls.

The present study in rats evaluates the anaesthetic properties of pregnanolone emulsion in relation to the requirements of the ideal intravenous anaesthetic as outlined recently by Dundee,[6] and compares its properties to those of Althesin, propofol, midazolam and thiopentone.

S. Høgskilde, MD, Resident, J. Wagner, MD, Resident, P. Carl, MD, Resident, M. Bredgaard Sørensen, MD, PhD, Chief Anaesthetist, Department of Anaesthesiology and Intensive Care, The Municipal Hospital of Copenhagen, DK 1399 Copenhagen K, Denmark.

This work was performed at the Department of Anaesthesiology and Intensive Care and the Department of Pathology, The Municipal Hospital of Copenhagen, Denmark.

0003–2409/87/101045 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Methods

Animals

Male and female Lewis rats, weight 150–350 g, were used for the investigation. The rats were placed in separate boxes during the tests and observed for 24 hours, after which they were sacrificed.

Drugs

Pregnanolone emulsion was formulated as pregnanolone 4 mg, soya bean oil 200 mg, acetyl triglycerides 70 mg, egg yolk phosphatides 18 mg, glycerol 17 mg with distilled water to a volume of 1 ml. The emulsion is isotonic, stable and has a pH of about 7.5. The mean particle size is in the region 0.2–0.5 μm and less than 3% of particles are larger than 1.0 μm.

Althesin was prepared by dissolving alphaxolone 9 mg and alphadolone 3 mg/ml in saline by addition of the solubilising agent Cremophor EL.

Propofol was administered in the recently introduced emulsion form (Diprivan) in which propofol is dissolved in soya bean oil and emulsified in a similar way to pregnanolone. The concentration of propofol in the emulsion was 10 mg/ml.

Midazolam contains the water-soluble benzodiazepine in a concentration of 5 mg/ml.

Thiopentone was administered in an isotonic 2.5% aqueous solution.

All anaesthetics were diluted when low dosage levels were tested, in order to minimise the possible error of injection of inaccurate volumes. Volumes were not less than 0.5 ml/rat. Pregnanolone, Althesin, midazolam and thiopentone were diluted with normal saline, and propofol with 10% Intralipid.

Testing procedures

Therapeutic index (TI). The therapeutic index, the relation between anaesthetic activity (AD) and acute toxicity (LD), was estimated for each of the five drugs. The criterion used to estimate AD was loss of the righting reflex for a minimum of 15 seconds following intravenous injection. LD was defined as lethality within 24 hours following injection. All injections were given via a tail vein with duration of delivery from 15 to 30 seconds.

Groups of eight rats (four male and four female) were tested at different dosage levels of each drug to determine the mean anaesthetic dose (AD_{50}) and the mean lethal dose (LD_{50}). The dosage limits where all or none of the rats in a batch were asleep, and the dosage limits where all or none of the rats in a batch died, plus at least three points between these limits, were established. AD_{50} and LD_{50} were then calculated by the method of Licthfield and Wilcoxon[7] and used to calculate the therapeutic index ($TI = LD_{50}/AD_{50}$).

Induction of anaesthesia. The speed of onset of anaesthesia was compared in groups of eight rats. Doses equal to 1.75 and 2 times AD_{50} were injected intravenously with durations of delivery of 5 and 15 seconds, respectively. The time from end of injection to loss of the righting reflex was noted. Excitation during the induction period was evaluated as the average score of the groups; the response was graded from 0 (no excitation) to 4 (convulsions) for each of the rats.

Sleeping time. The sleeping time, defined as duration of loss of the righting reflex, was determined in groups of eight rats. The median sleeping times following doses equal to 2 times AD_{50} were compared in five groups, one group for each drug.

Recovery. Recovery time was tested by the rotating rod test. Five groups of eight rats were trained to maintain their equilibrium for long periods of time on a rod 6 cm in diameter, which rotated with a speed of 6 r.p.m. Doses of the five anaesthetics equal to twice the AD_{50} were then administered and the time determined from when the rats regained the righting reflex until they were again able to maintain their equilibrium on the rotating rod for at least 60 seconds. Excitation during awakening and in the recovery period was evaluated as the average score for each group; the response was graded from 0 (no excitation) to 4 (convulsions) for each of the rats.

Movement. The thresholds to painful stimulation during anaesthesia were compared in five groups of eight rats given doses equal to half the LD_{50} of each drug. Pinching of the tail and of the legs was tested at various intervals and the response graded from 0 (no response) to 4 (awakening). Movement of unstimulated rats during sleep was generally noted throughout the experiments.

Infusion potentials. The cumulative effect of the five drugs was compared in five groups of eight rats given doses equal to 1.75 times AD_{50}. The same dose was repeated immediately after the rats regained the righting reflex. The sleeping time between successive injections was noted.

Local tissue tolerance. Signs of pain on injection and signs of vein damage within 72 hours after intravenous injection of doses equal to AD_{50} were compared in five groups of eight rats, one group for each drug. Signs of pain on injection and tissue necrosis inspected during the following 72 hours, after slow perivascular injection of 0.3 ml of each of the drugs in the mid-tail region, were compared in groups of eight rats.

Sex difference. A possible difference in the anaesthetic effect of pregnanolone between the sexes was evaluated. The AD_{50} and LD_{50} of males and females were calculated separately and the median sleeping times of 16 males and 16 females compared.

Statistical evaluation

The results were analysed statistically using the Mann–Whitney *U* test or the Kruskal–Wallis one-way analysis of variance by ranks for group comparison, and Dunn's multiple comparison procedure in cases with significance when the Kruskal–Wallis test was used. Significance was assigned at $p < 0.05$.

Results

The therapeutic index, AD_{50} and LD_{50} of the five anaesthetics are presented in Table 1. Pregnanolone has the highest therapeutic index, 6–8 times higher than that of midazolam, propofol and thiopentone and 50% higher than that of Althesin. The difference in the AD_{50} values of the two steroid anaesthetics is statistically significant ($p < 0.05$), whereas this is not the case for the difference in the LD_{50} values.

Table 2 shows the induction times and the incidence of excitation during the induction period. Pregnanolone was found to be a reliable induction agent with only minor excitatory side effects but with a slightly longer induction time than Althesin, propofol and thiopentone. Induction with midazolam was unreliable; induction time was longer and excitation more pronounced compared to the other agents.

Table 3 shows sleeping time, recovery time, the proportions of sleeping time to recovery time and the occurrence of excitation during the awakening and recovery period. Recovery was rapid with pregnanolone, Althesin and propofol, and slow with midazolam and thiopentone. The proportion of sleeping time to recovery time estimated for pregnanolone was significantly higher than the proportions estimated for the other anaesthetics ($p < 0.05$).

Movement of unstimulated rats during sleep was found to occur most frequently with pregnanolone and Althesin and the rats appeared to be more sensitive to noise than those that received the other drugs. The incidence of movement upon painful stimulation during anaesthesia is shown in Table 4. The response to pain was most pronounced with propofol and thiopentone, less with pregnanolone and midazolam and least with Althesin.

The sleeping times between successive bolus injections of the five drugs are given in Table 5. No cumulative effects were seen with the two steroids but a statistically significant increase in sleeping time appeared from the second to the eighth injection of propofol ($p < 0.01$). Sleeping times after the third dose of midazolam and thiopentone, were greater than 2 hours.

No sign of pain on injection or local tissue reaction at the injection site was observed following intravenous or perivascular administration of pregnanolone (Table 6). Perivascular injection of midazolam was found to be painful and 25% of the rats showed tissue necrosis.

Table 1. Anaesthetic dose (AD_{50}), lethal dose (LD_{50}) and therapeutic index (TI) of intravenously administered pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone in rats. Values expressed as mean (95% confidence interval; slope of regression line).

Substance	AD_{50}, mg/kg	LD_{50}, mg/kg	TI (LD_{50}/AD_{50})
Pregnanolone emulsion	1.25 (0.98–1.59; 1.28)	50.0 (42.0–59.0; 1.40)	40.0
Althesin	1.95 (1.57–2.42; 1.54)	56.0 (33.3–94.1; 1.59)	28.7
Propofol	6.10 (5.60–6.65; 1.16)	31.0 (27.0–35.7; 1.28)	5.1
Midazolam	18.50 (13.0–26.3; 1.86)	125.0 (91.2–171.3; 1.75)	6.8
Thiopentone	14.50 (10.4–20.2; 1.79)	66.0 (55.5–78.5; 1.37)	4.6

Table 2. Induction time and excitation during the induction period with pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone in groups of eight rats. Values expressed as median (range).

	$2 \times AD_{50}$, injection time 15 seconds		$1.75 \times AD_{50}$, injection time 5 seconds	
Substance	Induction time, seconds	Excitation*	Induction time, seconds	Excitation*
Pregnanolone emulsion	8 (0–15)	0.50	11 (5–25)	0.50
Althesin	0	0	3 (0–10)	0.75
Propofol	0	0.50	7 (0–10)	0.63
Midazolam	34 (0–90)	1.25	40 (0–80)	1.00
Thiopentone	0	0.75	0	0.50

* Average score in groups of eight rats; response graded from 0 (no excitation) to 4 (convulsions) for each rat.

Table 3. Sleeping times, recovery times, proportion of sleeping time to recovery time (ST/RT) and excitation during the recovery period following intravenous injection of pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone in groups of eight rats. Values expressed as median (range).

Substance	$2 \times AD_{50}$, mg/kg	Sleeping time, minutes	Recovery time, minutes	ST/RT	Excitation*
Pregnanolone emulsion	2.5	12.40 (7.2–18.0)	6.40 (3.2–11.2)	1.94	0.5
Althesin	3.9	8.00 (7.0–15.0)	9.00 (7.0–12.0)	0.89†	0.5
Propofol	12.2	6.90 (2.0–4.0)	5.38 (5.0–9.0)	1.28‡	0.5
Midazolam	37.0	33.00 (20.0–51.0)	279.00 (182–340)	0.12	1.0
Thiopentone	29.0	15.50 (7.0–39.0)	97.00 (76–152)	0.16	0.5

* Average score in groups of eight rats; response graded from 0 (no excitation) to 4 (convulsions) for each rat. † $p < 0.01$, ‡ $p < 0.05$, significant differences from pregnanolone emulsion.

Table 4. Movement upon stimulation* following intravenous bolus injection of pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone. Dose $LD_{50} \times 0.5$.

	Time following injection, minutes														
Substance	0.16	0.5	1	1.5	3	5	7	10	13	15	20	25	30	35	40
Pregnanolone emulsion	0	2	5	6	8	8	9	12	15	18	22	23	27	31	32
Althesin	0	0	0	0	3	6	8	13	14	15	17	17	23	31	32
Propofol	4	5	7	7	11	17	27	30	32						
Midazolam	1	0	1	5	8	10	10	14	20	24	30	32			
Thiopentone	7	10	11	14	14	15	15	17	17	20	21	24	27	32	

* Combined score for groups of eight rats; response graded from 0 (no response) to 4 (awakening) for each rat.

The difference in AD_{50} and sleeping time between the sexes was not statistically significant. The results are shown in Tables 7 and 8.

Discussion

Clinical use of steroid anaesthetics has, at present, been halted by problems related to their low solubility in water. To overcome this obstacle, a new approach which uses an oil-in-water emulsion in which the steroid is dissolved in the oil phase, appears promising.[4] The results described in the present experimental study with this new steroid preparation, pregnanolone emulsion, seem to support this conclusion.

The anaesthetic properties of this new agent were found to resemble those of Althesin, propofol and thiopentone, in that it is a reliable, rapidly acting agent which produces anaesthesia of short duration. The differences in induction time, excitation during induction and recovery, pain on injection and tissue damage following intravenous and perivascular injection, were only minor. The differences in anaesthetic therapeutic index were, however, considerable. That of pregnanolone emulsion was several times

Table 5. Sleeping times (minutes) between successive doses (1.75 × AD_{50}) of pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone. Median values.

Dose	Pregnanolone emulsion 2.2 mg/kg	Althesin 3.4 mg/kg	Propofol 10.7 mg/kg	Midazolam 32.4 mg/kg	Thiopentone 21.7 mg/kg
1	9.00	5.20	5.60	32.50	5.70
2	11.50	10.30	11.70	38.70	106.00
3	11.00	11.50	11.30	>240	>120
4	12.00	10.30	14.50		
5	10.00	13.20	14.70		
6	10.50	12.90	13.70		
7	11.50	11.50	17.10		
8	11.00	13.00	20.10		
9	10.00	11.70	22.50		
10	11.50	11.80	21.70		
11	11.50	11.70	23.00		
12	10.50	12.60	22.70*		

The increase in sleeping time from the first to the twelfth dose of propofol is statistically significant ($p < 0.01$), and that from the second to the eighth dose ($p < 0.01$).

Table 6. Local tissue tolerance: signs of pain on injection and tissue necrosis with intravenous and slow perivascular injection of pregnanolone emulsion, Althesin, propofol, midazolam and thiopentone in groups of eight rats.

	AD_{50} intravenous injection		0.3 ml undiluted perivascular injection	
Substance	Pain*	Necrosis†	Pain*	Necrosis†
Pregnanolone emulsion	0	0	0	0
Althesin	0	0	0.63	0
Propofol	0	0	0.5	1
Midazolam	0	2	2.25	2
Thiopentone	0	0	0.5	0

* Average score in groups of eight rats; response graded from 0 (no response) to 4 (struggling and shrieking) for each rat. † Number of eight rats with necrosis of the tail.

Table 7. Sex differences in anaesthetic dose (AD_{50}), lethal dose (LD_{50}) and therapeutic index (TI) of intravenously administered pregnanolone emulsion in male and female rats. Values expressed as mean (95% confidence interval; slope of regression line).

	AD_{50}, mg/kg	LD_{50}, mg/kg	TI (LD_{50}/A_{50})
Male	1.25 (1.07–1.46; 1.38)	50.0 (43.1–58.0; 1.16)	40.0
Female	1.30 (1.16–1.46; 1.54)	48.0 (41.4–55.7; 1.48)	36.9

Table 8. Sex difference in sleeping time in male and female rats with pregnanolone emulsion 4 mg/kg, 16 rats in each group. Values expressed as median (range).

	Males	Females
Sleeping time, minutes	20.00 (14.5–27.3)	17.15 (14.3–19.3)

higher than the index estimated for propofol and thiopentone, and 50% higher than that of Althesin. This reflects a statistically significant greater anaesthetic potency of pregnanolone emulsion compared to Althesin.

Movement of unstimulated rats did occur more often during anaesthesia with pregnanolone emulsion compared to propofol and thiopentone but it was no more pronounced than that seen with Althesin. The threshold to pain was higher following pregnanolone emulsion compared to propofol and thiopentone in doses of equivalent safety.

Recovery following anaesthesia with pregnanolone emulsion was very fast and the proportion of sleeping time to recovery time was more favourable than seen with the other anaesthetics. Cumulative effects were not seen on repeated bolus injections of either steroid, in contrast to both propofol and thiopentone.

The anaesthetic profile of midazolam was compared to the profile of the other four anaesthetics, without any advantages. Induction was less reliable, excitatory side effects and local tissue complications more pronounced and the cumulative effect and therapeutic index were similar to those seen with thiopentone.

In conclusion, it appears from this study in rats that the anaesthetic profile of pregnanolone emulsion in several aspects resembles Althesin. It may provide an alternative agent for intravenous anaesthesia that is less cumulative and less toxic than currently used intravenous anaesthetic agents.

Acknowledgments

The pregnanolone emulsion was kindly provided by KabiVitrum, Sweden. The authors wish to thank laboratory technicians O. Rasmussen, J. Kristensen and P. Rasmussen for their assistance in the laboratory.

References

1. Wright PJ, Dundee JW. Attitudes to intravenous infusion anaesthesia. *Anaesthesia* 1982; **37:** 1209–13.
2. Morgan M, Whitwam JG. Althesin. Editorial. *Anaesthesia* 1985; **40:** 121–3.
3. Glen JB, Davies GE, Thomson DS, Scarth SC, Thompson AV. An animal model for the investigation of adverse responses to i.v. anaesthetic agents and their solvents. *British Journal of Anaesthesia* 1979; **51:** 819–26.
4. Høgskilde S, Nielsen JW, Carl P, Sørensen MB. Pregnanolone emulsion. A new steroid preparation for intravenous anaesthesia. *Anaesthesia* 1987; **42:** 586–90.
5. Marker R, Kamm O. Isolation of pregnanolone from human pregnancy urine. *Journal of the American Chemical Society* 1937; **59:** 1373–4.
6. Dundee JW. Intravenous anaesthesia and the need for new agents. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 3–6.
7. Licthfield JT, Wilcoxon F. A simplified method of evaluating dose–effect experiments. *Journal of Pharmacology and Experimental Therapeutics* 1949; **96:** 99–113.

Anaesthesia, 1987, Volume 42, pages 1051–1056

Analgesia from morphine and ketamine

A comparison of infusions of morphine and ketamine for postoperative analgesia

H. OWEN, R. M. REEKIE, J. A. CLEMENTS, R. WATSON AND W. S. NIMMO

Summary

Ketamine 4 μg/kg/minute produced pain relief similar to that from morphine 33 μg/minute in a double-blind study that compared analgesia from constant-rate intravenous infusions of the two drugs in 60 patients. The analgesic efficacy of the infusions, as assessed by pain scores and the requirement for supplementary self-administered morphine, was poor. Ventilatory depression, the most significant side effect, occurred only in patients who received morphine infusion. The low dose ketamine infusion did not provide clinically useful analgesia even though adequate plasma concentrations were achieved.

Key words

Anaesthetics, intravenous; ketamine.
Analgesics, narcotic; morphine.

Acute pain can be abolished by the administration of ketamine in doses insufficient to induce anaesthesia.[1–3] Analgesia from a single bolus injection of ketamine is of short duration[3] and attempts have been made to provide continuous postoperative analgesia by an intravenous infusion of the agent.[4–7] In these studies ketamine provided pain relief but there were often side effects associated with the relatively high infusion rates used. It has been claimed that an infusion of ketamine at a rate of 3 μg/kg/minute (approximately 12 mg/hour) will achieve the steady-state plasma ketamine concentrations associated with analgesia (100–150 ng/ml) and may avoid unwanted effects.[8,9] This infusion rate was calculated from computer simulations based on peri-operative pharmacokinetic data from five patients. The technique is often quoted but there are no reports of the outcome of this low rate of administration of ketamine for pain control.

It was found in a pilot study on five patients, that an infusion of ketamine at 3 μg/kg/minute after a loading dose of 1 mg/kg was insufficient to maintain the required plasma concentration and that 4 μg/kg/minute might be more appropriate. We report the analgesic and some physiological effects of this dosage regimen after abdominal surgery.

Methods

The double-blind, parallel group study received ethical committee approval. Informed written

---

H. Owen, FFARCS, Senior Registrar, R.M. Reekie, BSc, MB, ChB, Registrar, J.A. Clements,* PhD, Lecturer, R. Watson, PhD, Biochemist, W.S. Nimmo,† MD, MRCP, FFARCS, Professor, University Department of Anaesthesia, Royal Infirmary, Glasgow G31 2ER.

* Heriot-Watt University, Edinburgh.

† University of Sheffield Medical School, Sheffield.

Correspondence should be addressed to H. Owen, Department of Anaesthesia and Intensive Care, Flinders Medical Centre, Bedford Park, South Australia 5042.

0003–2409/87/101051 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

consent was obtained from 60 patients scheduled for abdominal surgery. Patients with a history of hypertension, hepatic, renal or cardiac disease were not studied. Consecutive patients were allocated randomly to receive either ketamine ($n = 30$) or morphine ($n = 30$) for pain relief after surgery.

All patients received morphine 10 mg and atropine 0.6 mg intramuscularly one hour before induction of anaesthesia with thiopentone 4–5 mg/kg. Atracurium 0.4 mg/kg was administered to facilitate tracheal intubation and additional increments were given as required to maintain paralysis. The lungs were ventilated with nitrous oxide 66% and halothane 0.5–1% or enflurane 1–1.5% in oxygen. Before commencement of surgery patients received an intravenous bolus injection of ketamine hydrochloride 1 mg/kg followed by an infusion of 4 μg/kg/minute (approximately 16 mg/hour), or morphine sulphate 10 mg followed by an infusion of 33 μg/minute (approximately 2 mg/hour). The drugs were diluted in 5% dextrose solution and were infused at a constant rate for 24 hours from a Travenol infusor.[10]

At the end of surgery, residual neuromuscular blockade was antagonised by neostigmine (1.25–2.5 mg) and atropine (0.6–1.2 mg). Immediately after surgery each patient was attached to an On-Demand Analgesia Computer (ODAC, Janssen Scientific Instruments, Beerse, Belgium) which was programmed to deliver 1 mg increments of morphine sulphate in 5 ml dextrose 5% for supplementary analgesia. The lockout interval was 2 minutes, which gives a maximum permitted hourly dose of 30 mg, but the ODAC was set to warn attending staff when 12 mg had been demanded in one hour. Morphine for analgesia was self-administered throughout the period of infusion of ketamine or morphine and the number of demands satisfied every 4 hours was recorded. All patients were nursed by staff who were experienced in the management and monitoring of patients who receive patient-controlled analgesia.

Pain intensity, respiratory rate, pulse rate and systolic arterial pressure were recorded approximately 2.5, 7, 14 and 22 hours after surgery. Pain was measured on a four-point verbal rating scale (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain). All measurements were made by the authors. At each visit venous blood was collected from the antecubital fossa and the plasma separated and stored at −20°C for later analysis for ketamine by gas–liquid chromatography. After the infusion had been discontinued at the final visit each patient was questioned directly about dreams or hallucinations.

Ketamine analysis. Plasma samples were analysed for ketamine as the heptafluorobutyl derivative by gas–liquid chromatography using minor modifications of reported methods.[11,12]

Statistical analysis. Demographic data, systolic arterial pressure and pulse rate in the two treatment groups were compared using Student's *t*-test for unpaired data. Differences in pain scores for the two treatment groups were analysed using the Wilcoxon/Mann–Whitney

Table 1. Characteristics of study groups. Values expressed as mean (SD).

	Ketamine group	Morphine group
Age, years	47 (14)	46 (17)
Weight, kg	65 (12)	67 (13)
Sex, M:F	22:8	17:13
Surgery		
Upper abdominal	22	23
Lower abdominal	8	7

Table 2. Numbers of patients assessed at, and the time of, visits after surgery.*

	Visit			
	First	Second	Third	Fourth
Mean (SEM) time after surgery, hours	2.4 (0.1)	6.7 (0.3)	14.4 (0.6)	22.3 (0.2)
Ketamine group	30	30	30	28
Morphine group	25	27	27	24

* Five patients who received morphine were too sedated to be assessed at the first visit.

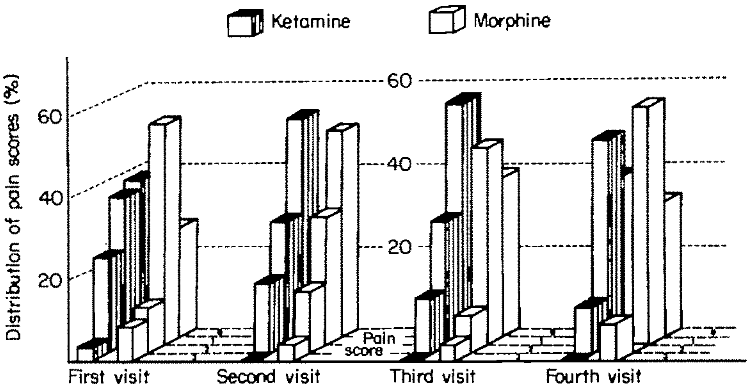


Fig. 1. Distribution of pain scores achieved by the two groups as a percentage of the total at each visit.

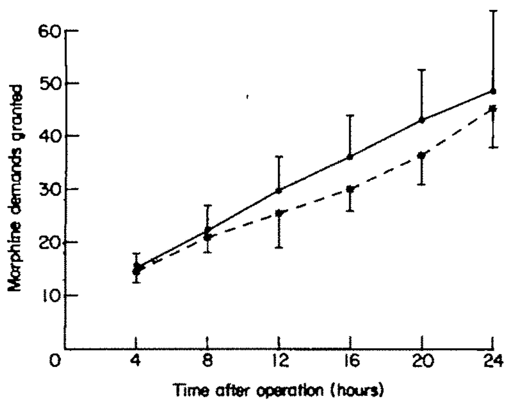


Fig. 2. Cumulative self-administered morphine by the two groups (mean, SEM). ● — ●, Morphine; * — *, ketamine.

test; the incidence of dreaming in the two groups was compared using the Chi-squared test with Yates' correction.

Results

Thirty patients were studied in each group. The groups were not different with respect to age, weight, or type of surgery (Table 1). The times of each visit and the number of patients who remained in each group at those times are listed in Table 2. Early withdrawals were due to side effects; the late withdrawals were because the Travenol infusor could be used for only 24 hours, in those patients for whom surgery lasted for more than 2 hours the infusion was completed before the last assessment.

Analgesia

All patients required supplementary analgesia and each rapidly became adept at the management of their own pain relief. The distribution of pain scores is shown in Fig. 1. The pain scores achieved were generally low and their distribution was similar in both groups during the analgesic infusion. The patterns of cumulative self-administered morphine consumption (Fig. 2) were similar for both groups but there was a large interindividual variation which was more marked in the morphine infusion group.

Respiration, cardiovascular variables and side effects

Respiratory rates are shown in Fig. 3. The patients who received morphine infusions had significantly lower respiratory rates than those who received ketamine infusions at both the first visit after surgery and the third visit ($p < 0.001$). At the fourth visit, both groups had mean respiratory rates that did not differ from those observed before surgery. These results include four patients who received the morphine infusion where respiratory rate decreased to below 8 breaths/minute and who were withdrawn from the study. These four were young males who had not appeared to demand more morphine than required for analgesia and in whom bradypnoea developed 4–10 hours after surgery. The differences remain significant even if these patients are excluded. There was no correlation between respiratory rate and pain scores with either treatment.

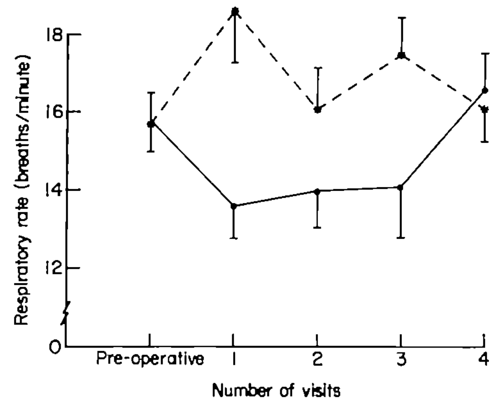


Fig. 3. Respiratory rates in the two groups (mean, SEM). ● — ●, Morphine; * — *, ketamine.

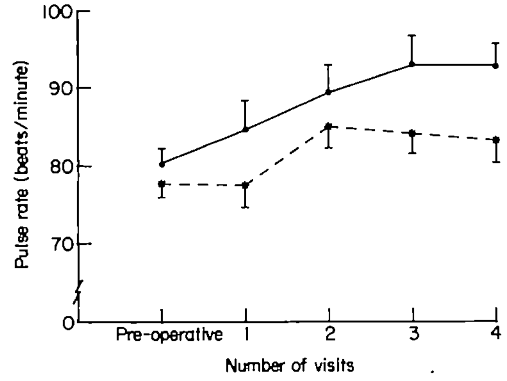


Fig. 4. Pulse rate in the two groups (mean, SEM). ● — ●, Morphine; * — *, ketamine.

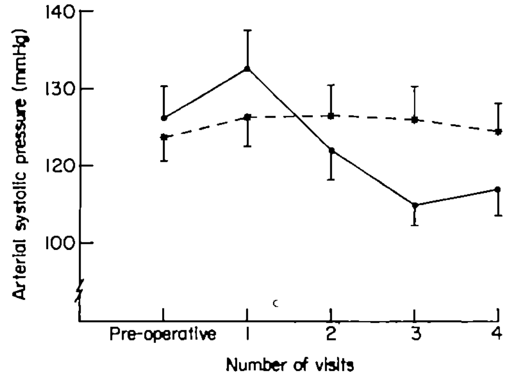


Fig. 5. Arterial systolic pressure in the two groups (mean, SEM). ● — ●, Morphine; * — *, ketamine.

Mean pulse rate and mean systolic arterial pressure in the two groups are shown in Figs 4 and 5. The patients who received ketamine infusions tended to have lower pulse rates than those who received morphine but the difference was significant only during the last 12 hours of observation. Systolic arterial pressure in the patients who received ketamine infusion changed little after surgery. In the patients who received morphine infusion, systolic arterial pressure had decreased at 14 hours in comparison both with the pre-operative value and with that for the ketamine group.

No patient reported dreams or hallucinations spontaneously but, on direct questioning, six patients who received ketamine and two who received morphine admitted that they had dreamt, although in no case was this described as unpleasant. One patient in the morphine infusion group suffered from delusions for the first few hours after surgery.

Pharmacokinetics

The mean infusion rate of ketamine was 3.9 μg/kg/minute (SD 0.31, range 2.9–4.5 μg/kg/minute) and this resulted in a mean plasma concentration of 179 ng/ml (SD 41, range 126–256 ng/ml). Most patients (26 out of 30) had achieved the target concentration of ketamine in plasma (150 ng/ml) by the first visit. A plasma concentration greater than this was maintained in 23 patients although it was still decreasing at 22 hours in 11 patients and, in one patient, had decreased to 93 ng/ml by the end of the infusion. Because fewer than half of the patients had achieved constant plasma concentrations for the majority of the infusion period, a value for plasma clearance of ketamine has not been reported.

Discussion

Constant-rate intravenous infusion of ketamine (4 μg/kg/minute) after surgery produced pain relief similar to that from an infusion of morphine (33 μg/minute). Traditionally, supplementary analgesia is administered by the attending nursing staff but there is a poor relationship between nurses' observations and patients' own reports of pain.[13]

Patient-controlled analgesia was developed originally to provide an objective measure of pain[14,15] and it was used in this way in the present study. However, because there is a large interindividual variability in analgesic demands after surgery, a large sample is required for any definite conclusions; the sample of 60 patients used in this study would seem to be sufficient. To make a valid comparison between two analgesic treatments the distribution of pain scores in the groups must be similar; even with patient-controlled analgesia supplementing background analgesia, some patients still experience moderate or even severe pain. The coarse verbal rating scale was chosen because of the unreliability associated with repeated measurements of pain after surgery and anaesthesia when a visual linear analogue scale is used.[16]

Supplementary analgesic requirements were similar in both groups but the respiratory rate tended to be lower in the group that received morphine: four patients of this group suffered marked bradypnoea. Patient-controlled analgesia alone is inherently safe but its use with a 'background' infusion warrants further investigation.

Ketamine analgesia may be mediated through interaction with opioid receptors.[17,18] From our measurement of respiratory rate it does not appear to be associated with ventilatory depression even when administered concurrently with on-demand morphine. In hypnotic doses, ketamine causes increased systolic arterial blood pressure and pulse rate. When compared with the morphine infusion group, this did not appear to occur at the ketamine dose rate used in this study. The overall incidence of dreaming was 15% but there was no significant difference between the treatment groups. This confirms the suggestion that some side effects of ketamine might be related to plasma concentration.[9]

The ketamine infusion rate used was one-third greater than that suggested by Nimmo and Clements;[8] the latter was based on simulations using data from five patients who received an infusion of ketamine for 6 hours after surgery. Most patients did not achieve constant plasma concentrations despite the long duration of ketamine infusion in this study. For this reason we were unable to calculate a reliable value of the total body clearance of ketamine. The progressive decrease of ketamine concentration observed in 11 patients was not due to extracorporeal loss of drugs. Ketamine concentrations have been measured in three infusors over 24 hours and there were no losses from adsorption onto plastic or latex (unpublished observation).

The infusion rate of ketamine used is substantially lower than that reported previously to provide analgesia. Clausen *et al.*[4] compared morphine (1 mg/hour), ketamine (1 mg/minute) and placebo by infusion for pain relief for 6 hours after surgery. No loading dose of either ketamine or morphine was given and, 2 hours later, morphine provided better analgesia than either ketamine or placebo; however, for the last 2 hours ketamine and morphine provided similar analgesia. Ito and Ichiyanagi[5] used a variable infusion of ketamine for pain relief for approximately 3 hours after surgery. A mean dose of approximately 25 μg/kg/minute generally gave adequate analgesia but heavy sedation was a problem and half the patients had dreams. The infusion rate of ketamine in both these studies[4,5] was sufficient to produce plasma concentrations associated with anaesthesia[19,20] if continued for long enough. In the present study ketamine infusion caused no side effects but it provided poor analgesia even though the appropriate plasma concentrations were attained.

The concentration of ketamine in plasma required to elevate the pain threshold significantly (100–150 ng/ml) was determined in experiments on anaesthetist volunteers.[3,9] Ketamine was compared with saline and it would obviously have been clear to the subjects when they received ketamine, with a consequent placebo effect.

In conclusion, we confirm a report that fixed-rate infusions of morphine are ineffective in the control of pain after surgery.[21] Also, there is no evidence to support the widely quoted recommendation that a low dose infusion of ketamine to achieve a plasma concentration over 100–150 ng/ml provides significant analgesia.

Acknowledgments

This work was supported in part by the Warner-Lambert Co., New Jersey. V. Scott provided invaluable statistical help. Dr L.E. Mather and Mrs G. Dow helped in the preparation of the manuscript.

References

1. Sadove MS, Shulman M, Hatano S, Fevold N. Analgesic effects of ketamine administered in subdissociative doses. *Anesthesia and Analgesia* 1971; **50**: 452–7.
2. Austin TR. Ketamine hydrochloride: a potent analgesic. *British Medical Journal* 1976; **2**: 943.

3. Clements JA, Nimmo WS, Grant IS. Bioavailability, pharmacokinetics, and analgesic activity of ketamine in humans. *Journal of Pharmaceutical Sciences* 1982; **71:** 539–42.
4. Clausen L, Sinclair DM, Van Hasselt CH. Intravenous ketamine for postoperative analgesia. *South African Medical Journal* 1975; **49:** 1437–44.
5. Ito Y, Ichiyanagi K. Post-operative pain relief with ketamine infusion. *Anaesthesia* 1974; **29:** 222–9.
6. Pandit SK, Kothary SP, Kumar SM. Low dose intravenous infusion technique with ketamine. Amnesic, analgesic and sedative effects in human volunteers. *Anaesthesia* 1980; **35:** 669–75.
7. Sher MH. Slow dose ketamine – a new technique. *Anaesthesia and Intensive Care* 1980; **8:** 359–61.
8. Nimmo WS, Clements JA. Ketamine on-demand for postoperative analgesia. *Anaesthesia* 1981; **36:** 826.
9. Grant IS, Nimmo WS, Clements JA. Pharmacokinetics and analgesic effects of I.M. and oral ketamine. *British Journal of Anaesthesia* 1981; **53:** 805–9.
10. Nimmo WS, Todd JG. Fentanyl by constant rate I.V. infusion for post-operative analgesia. *British Journal of Anaesthesia* 1985; **57:** 250–4.
11. Chang T, Glazko AJ. A gas chromatographic assay for ketamine in human plasma. *Anesthesiology* 1972; **36:** 401–4.
12. Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. *British Journal of Anaesthesia* 1981; **53:** 27–30.
13. Teske K, Daut RL, Cleeland CS. Relationships between nurses' observations and patients' self-reports of pain. *Pain* 1983; **16:** 289–96.
14. Sechzer PH. Objective measurement of pain. *Anesthesiology* 1968; **29:** 209–10.
15. Welchew EA. On-demand analgesia. A double blind comparison of on-demand intravenous fentanyl with regular intramuscular morphine. *Anaesthesia* 1983; **38:** 19–25.
16. Grossi E, Borghi C, Montanari M. Measurement of pain: comparison between visual analogue scale and analogue chromatic continuous scale. In: Fields HL, Dubner R, Cervero F, eds. *Advances in pain research and therapy, Vol. 9.* New York: Raven Press, 1985: 371–6.
17. Smith DJ, Pekoe GM, Martin LL, Coalgate B. The interaction of ketamine with the opiate receptor. *Life Sciences* 1980; **26:** 789–95.
18. Finck AD, Ngai SH. Opiate receptor mediation of ketamine analgesia. *Anesthesiology* 1982; **56:** 291–7.
19. Idvall J, Ahlgren I, Aronsen KF, Stenberg P. Ketamine infusions. Pharmacokinetics and clinical effects. *British Journal of Anaesthesia* 1979; **51:** 1167–73.
20. Audibert GB, Bulla G, Cosentino S, Palazzo G, Romano G, Zagami A. Concentrazione ematica di ketamina in fase di risveglio. *Minerva Anestesiologica* 1984; **50:** 55–7.
21. Marshall H, Porteous C, McMillan I, MacPherson SG, Nimmo WS. Relief of pain by infusion of morphine after operations: does tolerance develop? *British Medical Journal* 1985; **291:** 19–21.

Anaesthesia, 1987, Volume 42, pages 1057–1062

A comparison of the early pharmacokinetics of midazolam in pregnant and nonpregnant women

C. M. WILSON, J. W. DUNDEE, J. MOORE, P. J. HOWARD AND P. S. COLLIER

Summary

The early pharmacokinetics of midazolam were compared in pregnant (active labour, awaiting and during elective Caesarean section) and matched gynaecological patients scheduled to undergo elective hysterectomy, half of whom were given an oxytocin infusion. A standard dose of 5 mg was given intravenously. For the first 15 minutes patients in labour had significantly higher plasma midazolam levels compared to all other groups. This was associated with the largest area under the curve (2 hours), the smallest volume of distribution and lowest clearance. Midazolam when given immediately before Caesarean section, can result in depression of the infant.

Key words

Hypnotics, benzodiazepines; midazolam.
Pharmacokinetics.

Midazolam is a water-soluble benzodiazepine with a short distribution and elimination half-life[1] which has been used as a sedative and anticonvulsant in both pregnant and nonpregnant patients.[2] Pregnancy produces a number of striking physiological changes, notably an increase in plasma volume and a decrease in plasma protein concentration, which could modify drug disposition.[3] Additional physiological modifications occur at childbirth; their extent depends on the circumstances of delivery. As an example, the changes that occur during oxytocin-induced labour and delivery may be different from those that accompany an elective Caesarean section.

Midazolam is highly (96%) protein bound. It has an intermediate hepatic extraction ratio so that its rate of elimination depends in part on hepatic perfusion.[4] In addition, the volume of distribution of midazolam (Vd) has been shown to be greater in women than in men, and in obese than nonobese subjects.[5]

Since midazolam is likely to have an increasing use in obstetric practice, consideration of the above factors led us to compare its early pharmacokinetics in three groups of pregnant mothers: those in active labour, those undergoing elective Caesarean section under general anaesthesia and those awaiting Caesarean section. These were compared with two matched

---

C.M. Wilson, MB, FFARCS, Research Fellow, J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, J. Moore, MD, PhD, FFARCS, Honorary Senior Lecturer in Obstetric Anaesthesia, P.J. Howard, FIST, Chief Technician, Department of Anaesthetics, P.S. Collier, PhD, Senior Lecturer, Department of Pharmacy, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

0003–2409/87/101057 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

gynaecological groups both undergoing elective hysterectomy, one of which was given an infusion of oxytocin.

Methods

Healthy parturients selected for the study had a parity of four or less, were more than 38 weeks pregnant and with an uncomplicated obstetric history. The gynaecological patients were of comparable age. All patients gave informed consent and the investigation had the approval of the local medical ethical research committee. All patients received oral ranitidine 150 mg 2 hours prior to the administration of midazolam according to our current antacid regimen.[6] The obstetric patients remained supine with a left lateral tilt throughout the study.

The 5–mg dose was standard and given intravenously over 10 seconds. It was intended to have a minimum of 10 patients in each group. However, excessive drowsiness in two infants limited one Caesarean group to eight. The groups were: I, active labour induced by a dilute oxytocin infusion; II, undergoing elective Caesarean section under general anaesthesia, midazolam given 5 minutes pre-operatively; III, awaiting elective Caesarean section, midazolam given 3 hours pre-operatively; IV, undergoing abdominal gynaecological operations; V, as in IV but with an oxytocin infusion throughout the operation. Oxytocin was used in a dilute solution (10 units in one litre dextrose in water infused at 20 drops/minute, i.e. 8 ml/minute).

An indwelling venous cannula was placed in the forearm and 5 ml blood drawn from the contralateral arm before and at 2, 5, 10, 15, 30, 45, 60, 90 and 120 minutes after the administration of midazolam. Maternal and umbilical venous blood samples were also drawn from all pregnant patients at delivery. Blood was immediately centrifuged and the plasma stored at −20°C until plasma midazolam was estimated by gas–liquid chromatography[7] (the coefficient of variation of our method was 6.3% at 50 ng/ml and 4.0% at 100 ng/ml). The study was discontinued at 2 hours by which time the concentrations were lower than the sensitivity of our method of estimation.

General anaesthesia (thiopentone, suxamethonium, pancuronium, nitrous oxide–oxygen, halothane) was induced 5 minutes after midazolam administration in both gynaecological groups and in one of the Caesarean section groups. Each patient received one litre of Hartmann's solution infused slowly during the period of study. In the three obstetric series, the condition of the neonate was assessed by the Apgar scores at 1 and 5 minutes after delivery and the need for resuscitation noted.

Because of the relatively small dose, plasma levels of midazolam at times greater than 2 hours following administration were close to the limit of detection for the assay (1 ng/ml). The pharmacokinetic analyses were therefore confined to data obtained during this period. The area under the curve for the first 2 hours (AUC_{2h}) was calculated using the trapezoidal rule and the apparent elimination half-life ($t_{\frac{1}{2}}\beta$) was obtained from log–linear regression carried out on the terminal data points (45 minutes onwards). Standard noncompartmental methods were used to obtain estimates of clearance and apparent volume of distribution (Vd_{area}). Data were analysed using analysis of variance.

Results

The groups were broadly comparable with regard to age but, as expected, the patients in late pregnancy were significantly heavier than those scheduled to undergo gynaecological surgery (Table 1).

The mean plasma midazolam concentration was clearly higher initially in the patients in labour as compared with the other pregnant and nonpregnant women (Table 2). These results are shown on a logarithmic scale in Fig. 1, from which the standard errors are omitted for the sake of clarity. Mothers in labour continued to have significantly higher plasma levels than the other pregnant patients for the entire period of study ($p < 0.001$) and these were significantly higher than found in the matched gynaecological patients for the first 15 minutes of the study ($p < 0.05$–$p < 0.001$).

There was no significant difference in the mean plasma midazolam levels in those gynaecological patients who did and did not receive oxytocin (Fig. 2). Neither was there any difference in the two Caesarean groups awaiting and undergoing operation.

There was no significant difference in the apparent elimination half-life of midazolam between the groups (Table 3). Mothers in labour had the largest area under the curve in associa-

Table 1. Patient characteristics: values expressed as mean (SEM).

Group	*n*	Age, years	Weight, kg
I Labour	12	25 (1)	71 (3)
II Caesarean section	8	26 (2)	74 (3)
III Awaiting Caesarean section	10	25 (2)	73 (3)
IV Gynaecological	10	30 (2)	60 (5)
V Gynaecological/oxytocin	10	31 (2)	60 (3)

Groups I, II and III significantly heavier ($p < 0.05$) than groups IV and V.

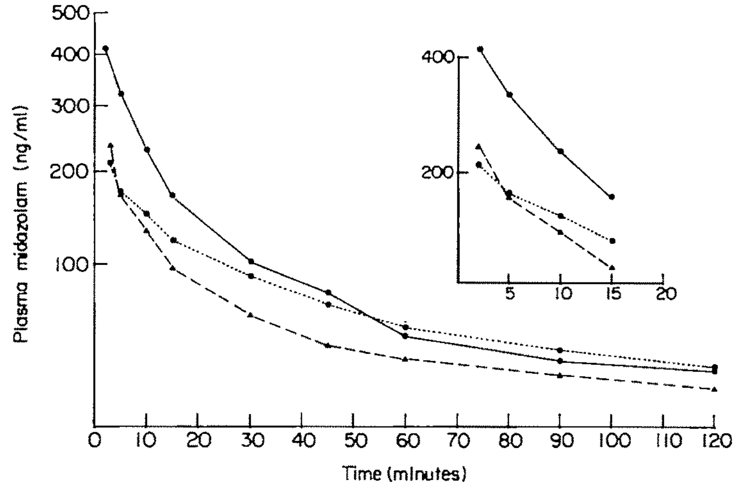


Fig. 1. Plasma midazolam levels (logarithmic scale) in the patients in labour (● —— ●), combined gynaecological (● ··· ●) and Caesarean section (▲ --- ▲) groups.

Table 2. Mean (SEM) plasma midazolam levels (ng/ml) in patients in labour, combined Caesarean section and combined gynaecological groups.

	Time, minutes		
Group	2	5	10
Labour	411 (23)	321 (32)	230 (23)
Caesarean	236 (18)	171 (13)	131 (8)
	$p < 0.001$	$p < 0.001$	$p < 0.001$
Gynaecological	212 (14)	175 (8)	150 (7)
	$p < 0.001$	$p < 0.001$	$p < 0.001$

Values of p refer to differences between the two groups and the patients in labour.

tion with the smallest volume of distribution and lowest clearance.

Two babies in the series given midazolam immediately before Caesarean section, required active resuscitation. When midazolam was given during labour and to patients awaiting Caesarean section the umbilical vein levels were lower (0–25 ng/ml) and there was no problem with these neonates (Table 4).

As the injection–delivery interval increases the umbilical vein/maternal vein plasma midazolam drug ratio decreases (Table 5). The short injection–delivery interval in one of the Caesarean section operative groups produced high umbilical vein plasma midazolam levels (30–110 ng/ml).

Discussion

The finding of unexpectedly high plasma midazolam levels in women given the drug when in active labour is of clinical importance, as the study was carried out in a real-life situation. One had hoped to use the drug clinically but, since diazepam has gained a bad reputation in this situation, it was felt that some studies of plasma levels should first be done to see if there was any excessively high concentration which might adversely affect the patients. The series of gynaecological patients was studied to enable us

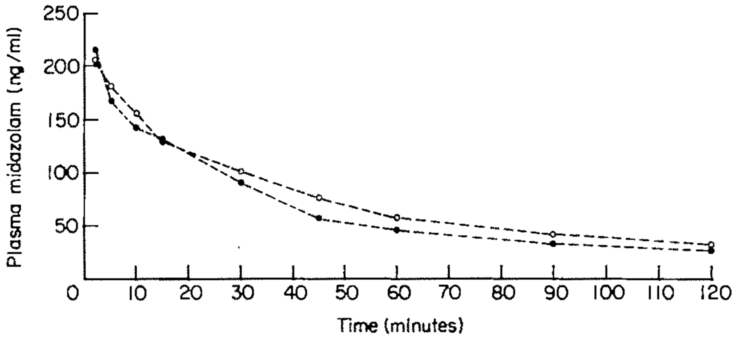


Fig. 2. Plasma midazolam levels in the gynaecological patients with (○) and without (●) oxytocin.

Table 3. Pharmacokinetic data from each group: values expressed as mean (SEM).

Group	$t_{\frac{1}{2}}\beta$, minutes	AUC_{2h}, minutes·ng/ml	Vd $_{area}$, litres/kg	Clearance, ml/minute/kg
I Labour	46 (4.5)	9695 (695)*	0.4 (0.06)**	6.5 (0.48)
II Caesarean section	47 (3.8)	4692 (402)	0.9 (0.05)	13.9 (2.08)***
III Awaiting Caesarean section	52 (2.5)	7077 (673)	0.7 (0.05)	9.0 (1.24)
IV Gynaecological	59 (6.2)	7493 (646)	0.8 (0.10)	8.7 (0.61)
V Gynaecological/oxytocin	57 (4.2)	8942 (489)	0.6 (0.05)	7.0 (0.65)

* Significantly higher than groups II ($p < 0.001$) and III and IV ($p < 0.05$).
** Significantly lower than groups II ($p < 0.01$) and IV ($p < 0.05$).
*** Significantly higher than all other groups ($p < 0.01$–0.001).

Table 4. Apgar scores in the parturient groups.

	1 minute			5 minute		
Group	<7	>8	Average	<7	>8	Average
Caesarean	5	3	5.8	2	6	7.8
Awaiting Caesarean	8	2	6.5	0	10	8.8
Labour	4	8	7.5	0	12	8.9

Table 5. Relationship between injection–delivery interval and umbilical vein/maternal vein drug ratio: values expressed as mean (SEM).

	Caesarean section		Labour
Injection–delivery interval, minutes	20.0 (1.8)	190.0 (9.6)	201.0 (28.3)
Plasma midazolam ratio	0.76 (0.07)	0.62 (0.11)	0.30 (0.09)

to evaluate our findings in a comparative manner.

The marked physiological changes associated with full term pregnancy affect the pharmacokinetic parameters of distribution and elimination of drugs. The increase in plasma volume, tissue fluid, hepatic metabolic activity, renal blood flow and plasma protein dilution, together with the cardiovascular change of increased cardiac output, all contribute but the exact part each plays is impossible to define. Furthermore, during labour without regional anaesthesia, dramatic cardiorespiratory variation occurs with each contraction while the stress factor produces metabolic change, and these further complicate interpretation of the findings. The results of the present study highlight the problem.

The clinical circumstances of imminent childbirth required that the dose of midazolam be limited to 5 mg. The method of analysis by gas–liquid chromatography limited the study to 2 hours since by this time, plasma midazolam levels approached the lower limit of sensitivity of this method. In addition, only the total drug plasma midazolam levels were measured, so any possible influence of protein binding could not be detected. It is also appreciated that the values referred to in Table 3 as $t_{\frac{1}{2}}\beta$ were based on a short study time and may have differed if plasma midazolam levels could have been followed for a longer period. However, it is important to note that this value did not show significant variation between the groups.

Since a dilute infusion of oxytocin did not significantly affect plasma midazolam values in the gynaecological patients it is unlikely to have played any part in the finding in the mothers in labour. The Caesarean section patients showed the expected change in pharmacokinetic parameters with a lower mean plasma midazolam concentration than the corresponding series of nonpregnant patients after the first 10 minutes (Fig. 1). We can offer no explanation for the markedly significant increase in clearance in those patients given midazolam immediately before anaesthesia for Caesarean delivery. However, it suggests that lateral tilt, as practised in these patients, effectively protects liver blood flow during surgery. The effect of closure of the placental circulation after delivery on the factors studied is unknown.

The unexpected finding is the marked increase detected in plasma concentrations during the first 15 minutes and AUC_{2h} in patients in active labour. The decrease in Vd could result from failure to maintain lateral tilt, with associated effects on organ perfusion, but it is more likely that the marked haemodynamic change associated with uterine contraction was the cause. Similar changes in these pharmacokinetic values have been described for pethidine (a high extraction ratio drug) given to patients in labour and these were attributed to alterations in cardiovascular function.[8] Midazolam, since it is highly protein bound, will be markedly affected by alterations in plasma protein binding. Ridd and colleagues[9] showed a decrease in protein binding of another benzodiazepine at delivery. However, Piafsky and Borga[10] reported that α_1 acid glycoprotein increased in the plasma during stress and that such variations correlated with large variations in binding of basic drugs. An increase in protein binding of midazolam may have contributed to our finding of a decrease in volume of distribution and clearance. The effects of the many variables associated with labour on liver blood flow[11] are a matter for conjecture but with an intermediate extraction ratio drug such as midazolam, a reduction in liver blood flow would be expected to cause a reduction in clearance.[12]

Midazolam is preferable to diazepam in that it is water-soluble, more anxiolytic and has a shorter half-life with no active metabolite. Nevertheless, the infant findings presented suggest that its administration a short period before anticipated delivery will increase the number of sleepy infants. It is readily transferred to the fetus but this investigation has shown that the umbilical vein/maternal vein ratio and umbilical vein concentration decrease as the administration–delivery interval increases. The pharmacokinetic profile of the drug changes in pregnancy. During active labour more dramatic alterations occur and these warrant further study.

Acknowledgments

We thank the staff in the Jubilee Labour Suite for their cooperation with this study. Dr C.M. Wilson was supported by a Department of Health and Social Services Research Fellowship.

References

1. Dundee JW, Halliday NJ, Harper KW, Brogden RN. Midazolam. A review of its pharmacological properties and therapeutic use. *Drugs* 1984; **28:** 519–43.
2. Kanto JH. Use of benzodiazepines during pregnancy, labour and lactation, with particular reference to pharmacokinetic considerations. *Drugs* 1982; **23:** 354–80.
3. Nation RL. Drug kinetics in childbirth. In: Gibaldi M, Prescott L, eds. *Handbook of clinical pharmacokinetics*. New York: Adis Health Science Press, 1983: 20.
4. Allonen H, Ziegler G, Klotz U. Midazolam kinetics. *Clinical Pharmacology and Therapeutics* 1981; **30:** 653–61.
5. Greenblatt DJ, Abernethy DR, Locniskar A, Harmatz JS, Limjuco RA, Shader RI. Effect of age, gender and obesity on midazolam kinetics. *Anesthesiology* 1984; **61:** 27–35.

6. McAuley DM, Moore J, McCaughey W, Donnelly DB, Dundee JW. Ranitidine as an antacid before elective Caesarean section. *Anaesthesia* 1983; **38:** 108–14.
7. Howard PJ, McClean E, Dundee JW. The estimation of midazolam, a water-soluble benzodiazepine, by gas liquid chromatography. *Anaesthesia* 1985; **40:** 664–8.
8. Morgan D, Moore G, Thomas J, Triggs E. Disposition of meperidine in pregnancy. *Clinical Pharmacology and Therapeutics* 1978; **23:** 288–95.
9. Ridd MJ, Brown KF, Moore RG, McBride NG, Nation RL. Diazepam plasma binding in the perinatal period. Influence of nonesterified fatty acids. *European Journal of Clinical Pharmacology* 1982; **22:** 153–60.
10. Piafsky KM, Borga O. Plasma protein binding of basic drugs. II. Importance of α_1 acid glycoprotein for interindividual variation. *Clinical Pharmacology and Therapeutics* 1977; **22:** 545–9.
11. Wilkinson GR. Pharmacokinetics of drug disposition: hemodynamic considerations. *Annual Review of Pharmacology* 1975; **15:** 11–27.
12. Wilkinson GR, Shand DG. A physiological approach to hepatic drug clearance. *Clinical Pharmacology and Therapeutics* 1975; **18:** 377–90.

Anaesthesia, 1987, Volume 42, pages 1063–1069

Intravenous sedation for cataract surgery

J. GILBERT, J. E. HOLT, J. JOHNSTON, B. A. SABO AND J. S. WEAVER

Summary

Fifty-five unpremedicated outpatients scheduled for cataract surgery were randomly allocated to receive either a fixed dose of nalbuphine and methohexitone or fentanyl and diazepam administered in a dose adjusted to produce the required sedative effect. Statistical analysis revealed no difference between groups with regard to immediate side effects, intra-ocular pressure or postoperative nausea or vomiting. Recovery time from administration of the sedative until compliance with simple commands was significantly longer in the nalbuphine/morphine group (89 vs 196 seconds) but this was not felt to be of clinical importance. This combination was better in terms of sedation at the time of insertion of the nerve blocks, lack of recall of insertion of the nerve block, incidence of intra-operative complications, surgeon's assessment of operating conditions and patient acceptability. This fixed dose by weight drug combination for intravenous sedation should be applied widely.

Key words

Analgesis; fentanyl, nalbuphine.
Hypnotics; diazepam, methohexitone.

There is increasing emphasis on surgery on an outpatient basis, where 60% of all operations are performed under local anaesthesia,[1] often with intravenous sedation to reduce medical costs. Many single and multiple drug sedative regimens have been advocated,[2–11] with varying success and incidence of complications.[11–15] In our own institution, fentanyl and diazepam administered slowly until the desired therapeutic effect is obtained (dosage-to-effect technique), has been the combination used most frequently for short procedures. Dosages administered per kg of body weight varied widely between patients, as did results, and complications were common. The objective of this study was therefore to determine if a fixed dose by weight drug combination of nalbuphine and methohexitone would give better results than the variable dose approach with fentanyl and diazepam.

Methods

The study population consisted of 60 unpremedicated outpatients, ASA grades 1–3, scheduled to undergo cataract surgery. Ages ranged from 18 to 90 years. The patients were otherwise unselected except that those with sensitivity to the study drugs, a history of hepatic or renal disease, and those receiving narcotic,

---

J. Gilbert, MB, BS, FFARCS, J.E. Holt, MD, Associate Professors, J. Johnston, MD, FFARCS, Clinical Assistant Professor, B.A. Sabo, CRNA, J.S. Weaver, CRNA, Anesthesia Nurse Specialists, Departments of Anesthesiology and Surgery, The University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, Texas 78284, USA.

0003–2409/87/101063 + 07 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

barbiturate or psychotropic drugs were excluded. The results of sedative administration were evaluated in all cases by the same investigator (J.G.) who, along with the surgeon, was unaware of the medication given. The study was approved by the Institutional Review Board and informed consent obtained in all cases.

Patients were allocated to the groups using a random number generator chart. All sedation and patient monitoring were conducted by anaesthesia personnel. Prior to the insertion of the facial and retrobulbar blocks the fentanyl/diazepam group (F/D) received, over the course of 2–3 minutes, an initial dose of fentanyl followed by diazepam in a total dose sufficient to produce drooping of the eyelids and lack of brisk response to simple commands. The nalbuphine/methohexitone group (N/M) received nalbuphine 0.1 mg/kg followed 3 minutes later by methohexitone 0.5 mg/kg. All drugs were administered intravenously via a freely flowing infusion of 5% dextrose in water, using a 18-gauge plastic cannula inserted into the upper extremity. Local anaesthesia was provided by 8–12 ml of a 50:50 mixture of 2% lignocaine and 0.75% bupivacaine, chosen and administered by the surgeon.

The degree of sedation was evaluated at the time of insertion of the nerve blocks, on the basis of the patient's response to the injections, persistence of the lid reflex, ability to obey simple commands and awareness of surroundings. Following administration of the sedation, blood pressure and pulse rate were recorded at one-minute intervals for a period of 5 minutes and any immediate side effects associated with drug administration were noted.

The length of time from administration of the diazepam or methohexitone until the patient could obey simple commands was recorded (recovery time). Intermittent firm digital pressure was applied to the eye for a period of 5 minutes after insertion of the retrobulbar block, to decrease the vitreous volume and disperse the local anaesthetic. Intra-ocular pressure was then recorded by means of Schiotz tonometry.

The development of any intra-operative complications was recorded and, if necessary, treated. At the conclusion of the procedure the surgeon was asked to rate the operative conditions as poor, fair or good. The surgeons stated that their determination was based substantially upon the presence or absence of intra-operative complications that arose from the sedative administration. The patients were also questioned at that time as to their recall of the insertion of the nerve blocks and, if recall was present, how painful that insertion was. Where a patient could recall pain, it was graded on a scale of 0–5 (0, no pain; 5, the worst pain imaginable).

At the time of the first postoperative visit, which always occurred within 24 hours of completion of the surgery and while the surgery team was still unaware of the drug combination used, the patients were asked to rate their anaesthetic and operative experience. In addition, they were questioned about the occurrence of nausea and/or vomiting in the 4 hours following discharge from the operating room.

The data were analysed using Student's *t*-test and Chi-square analysis; statistical significance was assessed at $p < 0.05$.

Results

Of the 60 patients entered into the study, five were excluded after entry into the operating room, for the following reasons: therapeutic intervention undertaken prior to administration of sedation, in order to treat an arterial diastolic pressure greater than 100 mmHg or systolic pressure more than 30 mmHg above the patient's baseline established at pre-operative clinic visits (2 patients); diazepam sensitivity recalled after

Table 1. Patient description.

	Fentanyl/diazepam (*n* = 28)	Nalbuphine/methohexitone (*n* = 27)
Mean (SD) age, years	67.0 (10.8)	67.4 (9.4)
Mean (SD) weight, kg	73.9 (15.7)	73.7 (14.7)
Mean (SD) duration of surgery, minutes	84 (27.3)	76 (31.0)
ASA grade (% of total)		
1	7	7
2	82	85
3	11	8

admission to the study (1); excessive somnolence after diazepam administration, which required conversion to general anaesthesia (1); and a failed retrobulbar block (1). Both groups were comparable in all respects (Table 1) and the drug dosages used are shown in Table 2.

Table 2. Mean (SD) drug dosages.

Drug	Dose
Fentanyl, μg	71.25 (29.11)
Diazepam, mg	4.71 (1.88)
Nalbuphine, mg	7.30 (1.61)
Methohexitone, mg	36.44 (7.95)

The degree of sedation was much more pronounced in the N/M group (Fig. 1) and yet, despite this greater degree of sedation, there were no significant differences between the two groups in cardiovascular variables or immediate side effects (Table 3) and no treatment was required. The recovery time was 89 seconds (SE 16.4) in the F/D group and 196 seconds (SE 20.6) in the N/M group ($p < 0.001$). Intraocular pressure was 7.5 mmHg (SE 0.34) in the F/D group and 7.6 mmHg (SE 0.34) in the N/M group (difference not significant).

There was better acceptance of the operative conditions by the surgeon for the N/M group (Fig. 2), due largely to the lower incidence of intra-operative complications (Fig. 3). Two patients required additional sedation during the procedure and both were in the F/D group.

Very few of the patients in the N/M group could recall insertion of the nerve block (Fig. 4) and, as a result, only 7% of these patients recalled experiencing pain compared to 21% in the F/D group. All patients rated their pain experience at 3 or less.

Patient acceptability of the anaesthetic technique was assessed 24 hours postoperatively; 43% of patients in the F/D group and 74% in the N/M group were very pleased with their anaesthetic experience (Fig. 5). There was no statistically significant difference between the two groups ($p = 0.46$) in the incidence of postoperative nausea and vomiting.

Discussion

The combination of methohexitone and nalbuphine was chosen because of our favourable previous experience with the use of methohexitone prior to various nerve blocks for painful surgical procedures of brief duration, such as the field block for rhinoplasty and submucous resection, facial and retrobulbar blocks for cataract extraction or radiofrequency coagulation of the Gasserian ganglion. The dosage of methohexitone in these usages varied between 0.75 and 1.0 mg/kg.

Reported side effects of methohexitone have included pain upon injection, excitation, hiccoughing, cardiorespiratory depression and slow recovery of consciousness.[16] Fentanyl administered prior to methohexitone often, in our experience, exacerbated the respiratory depression. The principal reason for the use of methohexitone was to take advantage of the profound sedation and amnesia that it produces, which permit stress-free insertion of nerve blocks. The side effects of methohexitone are dose dependent. It was therefore considered that the addition of an analgesic drug with minimal additional side effects might enable a lower dose of methohexitone to be used and achieve the

Table 3. Percentage incidence of immediate side effects.

	Fentanyl/diazepam	Nalbuphine/methohexitone
Pain with narcotic injection	0	4
Pain with injection of sedative	14	11
Movement during insertion of nerve block	36	19
Excitation	7	7
Minor respiratory obstruction (snoring)	18	15
Vomiting	4	4
Dysphoria	4	0
Heart rate increase (>20 beats/minute)	0	4
Heart rate decrease (>20 beats/minute)	11	0
Systolic pressure increase (>20 mmHg)	14	7
Systolic pressure decrease (>20 mmHg)	57	44

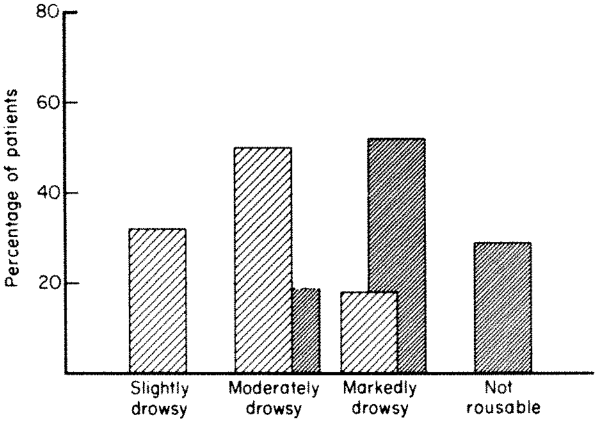


Fig. 1. Degree of sedation at the time of insertion of the nerve blocks. ▨, Fentanyl/diazepam; ▩, nalbuphine/methohexitone. p = <0.0001 *vs* fentanyl/diazepam group.

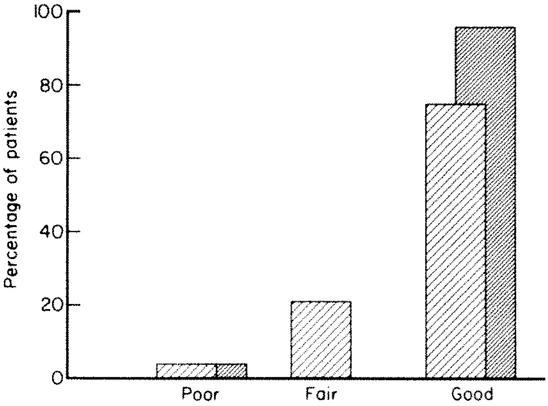


Fig. 2. Surgeon's assessment of operating conditions. ▨, Fentanyl/diazepam; ▩, nalbuphine/methohexitone. p = 0.0385 *vs* fentanyl/diazepam group.

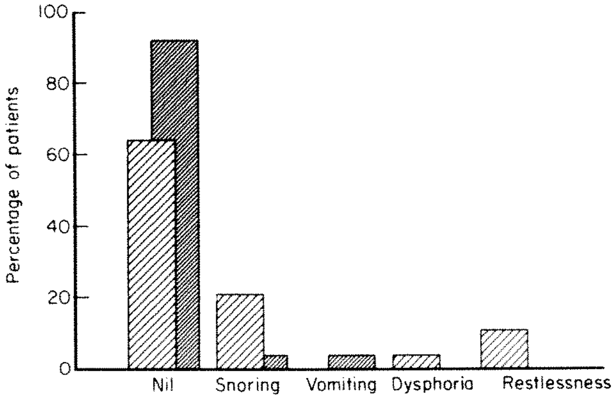


Fig. 3. Incidence and type of intra-operative complications. ▨, Fentanyl/diazepam; ▩, nalbuphine/methohexitone. p = 0.012 *vs* fentanyl/diazepam group (complications present or absent).

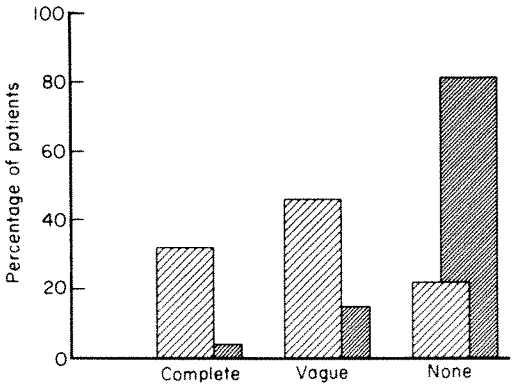


Fig. 4. Patient recall of nerve block insertion. ▨, Fentanyl/diazepam; ▩, nalbuphine/methohexitone. p = <0.0001 *vs* fentanyl/diazepam group.

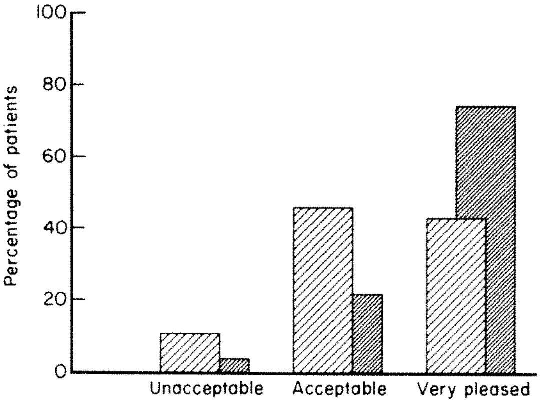


Fig. 5. Patient rating of sedation 18–24 hours after surgery. ▨, Fentanyl/diazepam; ▩, nalbuphine/methohexitone. p = 0.019 *vs* fentanyl/diazepam group (very pleased *vs* other).

same end result but with a lower incidence of side effects.

Nalbuphine was used in conjunction with methohexitone because it is a mixed agonist/antagonist, structurally related to the narcotic oxymorphone and the narcotic antagonist naloxone.[17] Its potency and duration of action are similar to morphine[18] but with fewer adverse haemodynamic effects,[19] less respiratory depression[20] and a minimal effect on cardiac function.[21]

The N/M technique is not 'conscious sedation' as defined by the American Dental Society of Anesthesiology,[22] and which requires verbal contact to be maintained with the patient at all times, because 81% of patients in the N/M group fell into the 'markedly drowsy' or 'not rousable' category (Fig. 1) according to the criteria for assessment of sedation outlined in the Methods section. Despite this quite profound degree of sedation, however, there was no increase in cardiovascular instability or minor respiratory obstruction as compared to the less heavily sedated patients in the F/D group (Table 3), nor did the inability of many patients to cooperate compromise the success of the block insertion. The technique appears to be both safe and reliable in this dosage combination and, although patients have a longer recovery time, this was not of clinical significance.

Intra-operative complications were noticeably less in the N/M group (Fig. 3) but the occurrence of intra-operative vomiting was certainly alarming. It was treated with droperidol 0.625 mg intravenously with good effect and no surgical complications developed. We have subsequently used this technique on over 200 additional patients without recurrence of this complication.

The other therapeutic aspect evaluated was the dosage-to-effect approach to sedation compared with standardised dosage by weight. When potent sedative and narcotic drugs are used in an elderly patient population it is certainly reassuring to administer small intravenous doses repeatedly until the desired therapeutic effect is achieved, and thus limit adverse side effects. This approach introduces considerable variability in sedation since the endpoint is not clearly defined. The depth of sedation obtained is influenced by individual variations among anaesthetists and surgeons as to what the patient can tolerate and what constitute good operating conditions, the speed of administration of drugs and the confidence of the personnel in their ability to treat any complications that may arise. The results obtained with a drug combination that was associated with minimal complications and was reliable in its sedative effect, demonstrate that the dosage-by-weight approach eliminates the vagaries in outcome that we had earlier documented with the F/D combination administered to effect.

Nalbuphine 0.1 mg/kg followed 3 minutes later by methohexitone 0.5 mg/kg produced safe and reliable sedation for cataract surgery. The technique may be applicable in other situations where brief but profound sedation is required. Because the possibility of greater than anticipated sedation associated with the use of methohexitone does exist, the technique should be used only by medical personnel trained in resuscitation and maintenance of a clear airway.

Acknowledgment

The authors thank Dr J. Hughes, Chief Resident in Ophthalmology, for her assistance in the completion of this study.

References

1. Janis KM. Outpatient anesthesia in a geriatric setting. *International Anesthesiology Clinics* 1982; **20:** 89–97.
2. Ceravolo FJ, Myers H, Baraff LS, Bennett CR. Full dentition periodontal surgery utilizing intravenous conscious-sedation. *Journal of Periodontology* 1980; **51:** 462–4.
3. Flanagan L Jr, Bascom JU. Herniorrhaphies performed upon outpatients under local anesthesia. *Surgery, Gynecology and Obstetrics* 1981; **153:** 557–60.
4. Pierce HE. An effective method of inducing analgesia and anesthesia for dermatoplastic surgery in an office. *Journal of Dermatological and Surgical Oncology* 1981; **7:** 495–6.
5. Tobin HA. Low-dose ketamine and diazepam. Use as an adjunct to local anesthesia in an office operating room. *Archives of Otolaryngology* 1982; **108:** 439–40.
6. Korttila K, Tarkkanen L, Aittomäki J, Hyöty P, Auvinen J. The influence of intramuscularly administered pethidine on the amnesic effects of intravenous diazepam during intravenous regional anaesthesia. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 323–7.
7. Klein DS. Nalbuphine and droperidol combination for local standby sedation. *Anesthesiology* 1983; **58:** 397.
8. Hofmann RF, Weiler HH. Lorazepam and nalbuphine as local anesthetic ophthalmic surgery premedications. *Annals of Ophthalmology* 1983; **15:** 64–6.
9. Steele PR, Masheter HC. Phenoperidine and droperidol as premedicants. A controlled study in ophthalmic surgical procedures in combination with retrobulbar block. *Anaesthesia* 1971; **26:** 311–7.
10. Jones WM, Samis WD, Macdonald D, Boyes HW. Anesthesia for intraocular surgery. *Canadian Journal of Ophthalmology* 1968; **3:** 337–41.
11. Dixon RA, Bennett NR, Harrison MJ, Kenyon C, Thornton JA. IV flunitrazepam and IV diazepam in conservative dentistry. *British Journal of Anaesthesia* 1980; **52:** 517–26.
12. Jones WM, Samis WD, Macdonald D, Boyes HW. Neuroleptanalgesia for intraocular surgery. *Canadian Anaesthetists' Society Journal* 1968; **15:** 491–7.
13. Hegarty JE, Dundee JW. Sequelae after the intravenous injection of three benzodiazepines—diazepam, lorazepam, and flunitrazepam. *British Medical Journal* 1977; **2:** 1384–5.
14. Siebke H, Ellertsen BB, Lind B. Reactions to intravenous injections of diazepam. *British Journal of Anaesthesia* 1976; **48:** 1187–9.
15. Wine NA. Sedation with neuroleptanalgesia in cataract surgery. *American Journal of Ophthalmology* 1966; **61:** 456–60.
16. Wood M. Intravenous anesthetic agents. In: Wood M, Wood AJJ, eds. *Drugs and anesthesia. Pharmacology for anesthesiologists.* Baltimore: Williams & Wilkins, 1982: 217–9.
17. Blumberg H, Dayton BH, Wolf PS. Analgesic properties of the narcotic antagonist EN-2234 A. *Pharmacologist* 1968; **10:** 189.
18. Beaver WT, Feise GA. A comparison of the analgesic effect of intramuscular nalbuphine and

morphine in patients with postoperative pain. *Journal of Pharmacology and Experimental Therapeutics* 1978; **204:** 487–96.

19. Romagnoli A, Keats AS. Comparative hemodynamic effects of nalbuphine and morphine in patients with coronary artery disease. *Bulletin of Texas Heart Institute* 1978; **5:** 19–24.
20. Romagnoli A, Keats AS. Ceiling effect for respiratory depression by nalbuphine. *Clinical Pharmacology and Therapeutics* 1980; **27:** 478–85.
21. Lee G, Low RI, Amsterdam EA, DeMaria AN, Huber PW, Mason DT. Hemodynamic effects of morphine and nalbuphine in acute myocardial infarction. *Clinical Pharmacology and Therapeutics* 1981; **29:** 576–81.
22. Bennett CR. *Conscious-sedation in dental practice.* St. Louis: C.V. Mosby, 1974: 14.

Anaesthesia, 1987, Volume 42, pages 1070–1073

Local tissue oxygenation following radial artery cannulation

J. M. MURRAY AND A. MOWBRAY

Summary

The effect of radial artery cannulation on local tissue oxygenation and acid–base balance was studied in 20 patients. Using capillary samples drawn from each thumb, a significant difference was observed between capillary $P\text{O}_2$ *on each side* ($p < 0.001$)*, with the higher* $P\text{O}_2$ *on the cannulated side. There were no significant differences between sides in terms of* $[\text{H}^+]$ *or* $P\text{CO}_2$*. It is considered that the differences in capillary* $P\text{O}_2$ *were due to local tissue vasodilatation. The presence of chlorbutol in the sodium heparin flushing solution is implicated as the causative factor. Further study of 20 patients using preservative-free heparin demonstrated no significant differences between cannulated and non-cannulated sides in terms of capillary* $P\text{O}_2$*,* $P\text{CO}_2$ *or* $[\text{H}^+]$*. Sodium heparin with chlorbutol appears to improve local tissue oxygenation and is recommended for use in flushing solutions for invasive arterial monitoring.*

Key words

Equipment; catheters, arterial.

Cannulation of the radial artery is a simple, convenient, low risk, high benefit technique of invasive arterial pressure monitoring.[1] The procedure is widely applied during major surgery and in the intensive therapy unit. The technique of invasive arterial monitoring allows continuous observation of the systemic blood pressure and convenient access for arterial blood gas analysis.

Permanent ischaemic sequelae are rare following radial artery catheterisation but reports that describe the occurrence of such damage have been published.[2–4] Most of these cases were associated with additional features such as emboli originating from a proximal site,[5] prolonged hypotension,[6] prior vascular disease[3] or hyperlipoproteinaemia.[7] Strict attention to aseptic technique, avoidance of multiple punctures and the use of short, 20-gauge, teflon catheters all contribute to a reduction of morbidity.

Many factors have therefore been implicated in complications of radial artery cannulation. The objective of this investigation was to determine whether changes occur in local tissue oxygenation, carbon dioxide elimination and hydrogen ion concentration during uncomplicated intra-arterial monitoring.

Patients and methods

The study was divided into three parts. Initially, 20 adult patients (aged 18–70 years, 14 male) were examined, all of whom had been admitted to the intensive therapy unit for specialist care. These patients had a radial artery catheter inserted for invasive monitoring and ease of access for arterial blood gas analysis. Only short, 20-gauge, teflon cannulae were used and all

---

J.M. Murray, MB, BCh, BAO, FFARCSI, A. Mowbray, BSc, MB, ChB, FFARCS, Visiting Lecturers in Anaesthesia. Department of Anaesthesia, Chinese University of Hong Kong, Shatin N.T., Hong Kong.

Correspondence should be addressed to Dr A. Mowbray, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh.

0003–2409/87/101070 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

cannulations were performed under strict aseptic conditions. Allen's test was not employed prior to cannulation.

Throughout this part of the study the patency of the cannula of each patient was maintained using a continuous flush system (Intraflo) delivering 3 ml/hour of a standard flushing solution that contained 500 ml 0.9% saline with 500 IU sodium heparin (Leo sodium heparin 1000 IU/ml with 5 mg/ml chlorbutol).

Arterialised capillary samples (65 μl) were drawn daily for 6 days from both cannulated and non-cannulated sides using standard techniques. The thumb on each hand was chosen in every case as the site for capillary sampling. Before the procedure, each limb was exposed to room temperature for 15 minutes. Capillary $P\text{O}_2$, $P\text{CO}_2$ and [H+] from both sides were analysed using an Instrument Laboratory (IL 1303) blood gas analyser.

The second part of the study was undertaken on a further 20 patients (aged 4–83 years, 10 male) in the intensive therapy unit. However, calcium heparin was substituted for sodium heparin as the anticoagulant in the continuous flush system. The calcium heparin was preservative-free and contained no chlorbutol. Arterialised capillary samples were drawn from each thumb (cannulated side and non-cannulated side). However, due to time constraints, it was not possible to sample each patient daily for 6 days. As a result, the number of samples in each patient ranged from one to six.

Finally, 20 adult patients (aged 18–70 years, 14 male) were selected at random. These patients were scheduled for elective surgery during which no arterial cannulation was to be performed. Capillary samples were drawn from each thumb and analysed in the manner described above.

Results were analysed using a two-tailed *t*-test.

Results

In patients who received sodium heparin flush, the capillary $P\text{O}_2$ on the cannulated side was significantly higher than that on the non-cannulated side ($p < 0.001$). There were no significant differences between sides in respect of $P\text{CO}_2$ or [H+]. The ratio of cannulated to non-cannulated $P\text{O}_2$ was almost invariably greater than unity (Fig. 1).

Analysis of the results from the patients in the calcium heparin group (preservative-free) showed no statistical differences between cannulated and non-cannulated samples in respect of $P\text{O}_2$, $P\text{CO}_2$ and [H+]. The ratios of cannulated to non-cannulated $P\text{O}_2$ were more evenly spread

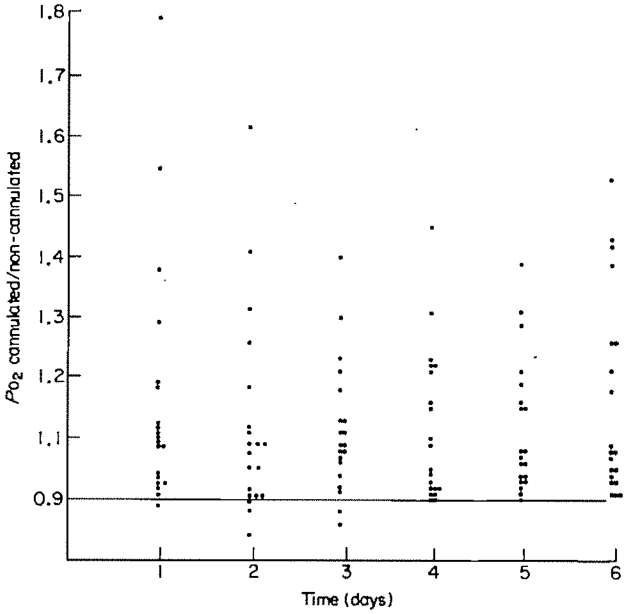


Fig. 1. $P\text{O}_2$ cannulated/$P\text{O}_2$ non-cannulated for sodium heparin.

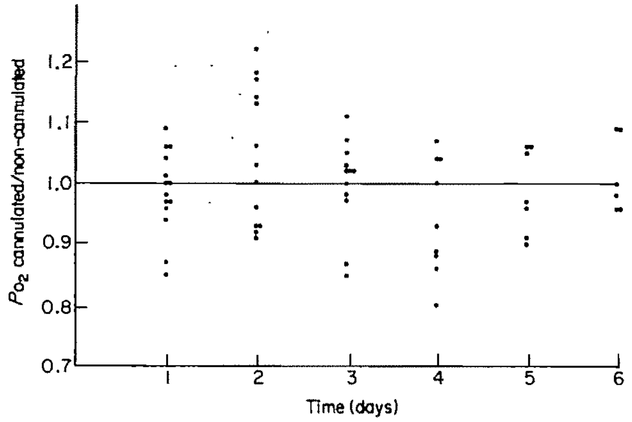


Fig. 2. Po_2 cannulated/Po_2 non-cannulated for calcium heparin.

Table 1. Sodium heparin versus calcium heparin: comparison of cannulated/non-cannulated Po_2 ratios, with results of Chi-squared test (Yates' correction).

	Ratio		
	< 1	≥ 1	Total
Calcium heparin	29	34	63
Sodium heparin	5	115	120
(chlorbutol)	—	—	—
Total	34	149	183

$\chi^2 = 45.136$, $p \ll 0.001$.

on either side of unity (Fig. 2). There was a significant difference ($p < 0.001$) between groups in respect of the number of patients whose cannulated to non-cannulated Po_2 ratio was equal to or greater than one (Table 1).

In the patients in whom no arterial cannula was inserted, there were no significant differences in measured variables between left and right sides. There was a close relationship ($r = 0.98$) between the values of Po_2 measured from left and right sides (Fig. 3).

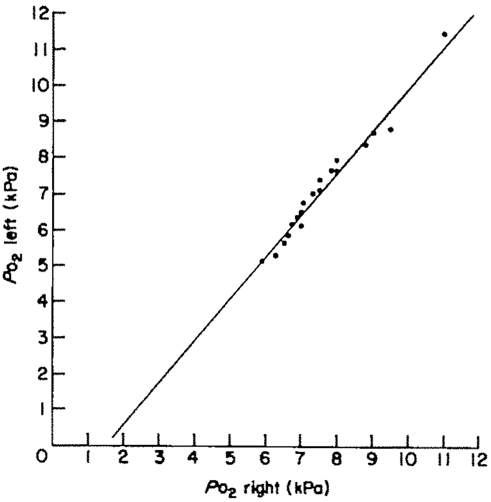


Fig. 3. Po_2 left versus right for controls.

Discussion

The aim of this study was to examine the effect of radial artery catheterisation on local tissue oxygenation and acid–base balance. Insertion of a radial artery cannula may cause spasm of the vessel, can result in displacement of arteriosclerotic plaques and has been associated with thrombosis following injury to the intima.[8,9] It must be stressed that the cannulations in this study were not performed under conditions in which permanent ischaemic damage has been reported to occur, such as emboli arising from the heart, prolonged circulatory failure with vasopressor therapy and hyperlipoproteinaemia.[5–8] It is of interest that in reports of tissue ischaemia following radial artery cannulation, the area of necrosis did not arise from, nor remain limited to, the tissue uniquely dependent on radial artery blood flow.

In the present study, Allen's test was not employed prior to cannulation of the radial artery. The test is designed not to predict ischaemic damage but to assess the palmar collateral circulation.[10] The value of Allen's test in the prediction of potential ischaemic damage after catheterisation is currently in doubt following several reports of tissue necrosis in patients who had normal results with Allen's test.[2,3,7] Furthermore, the test is associated with a 0.8% incidence of false positive and a 53% incidence of false negative results.[11]

Other methods of assessing the collateral circulation have been described. These include Doppler ultrasonic probes,[11,12] plethysmography[13] and pulse oximetry.[14] These have the advantage of not requiring patient cooperation. However, like Allen's test, they assess only the adequacy of ulnar collateral flow and do not predict ischaemic damage. They are also associated with false positive and negative observations. Capillary Po_2 may offer a more sensitive guide to local tissue oxygenation.

Chlorbutol has recently been reported to cause a sharp decrease in arterial pressure during heparin administration before cardiopulmonary bypass.[15] Chlorbutol is added to sodium heparin because of its bactericidal and fungicidal properties. It is also a vasodilator and a mild sedative. It has a long elimination half-life (10.3 days) and accumulates with repeated administration. The calculated dose of chlorbutol administered via the flushing system was 15 μg/hour.

We conclude that heparin solution containing chlorbutol is the anticoagulant of choice in flushing systems for arterial cannulae. It is possible that a downward trend in capillary Po_2 distal to the site of cannulation may be an indication to remove the cannula.

Acknowledgments

We thank Professor J.A. Thornton for his helpful advice and support and also Miss B. Li and Miss T. Wong for typing the manuscript.

References

1. Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. *Anesthesiology* 1983; **59:** 42–7.
2. Mangano DT, Hickey RF. Ischemic injury following uncomplicated radial artery catheterisation. *Anesthesia and Analgesia* 1979; **58:** 55–7.
3. Katz AM, Birnbaum M, Moylan J, Pellett J. Gangrene of the hand and forearm: a complication of radial artery cannulation. *Critical Care Medicine* 1974; **2:** 270–2.
4. Wyatt R, Glaves I, Cooper DJ. Proximal skin necrosis after radial artery cannulation. *Lancet* 1974; **1:** 1135–8.
5. Samaan HA. The hazards of radial artery pressure monitoring. *Journal of Cardiovascular Surgery* 1971; **12:** 342–7.
6. Baker RJ, Chunprapaph B, Nyhus LM. Severe ischemia of the hand following radial artery catheterisation. *Surgery* 1976; **80:** 449–57.
7. Cannon BW, Meshier WT. Extremity amputation following radial artery cannulation in a patient with hyperlipoproteinemia type V. *Anesthesiology* 1982; **56:** 222–3.
8. Bedford RF, Wollman H. Complications of percutaneous radial artery cannulation: an objective prospective study in man. *Anesthesiology* 1973; **38:** 228–36.
9. Downs JB, Rackstein AD, Klein EF Jr, Hawkins IF Jr. Hazards of radial-artery catheterisation. *Anesthesiology* 1973; **38:** 283–6.
10. Allen EV. Thromboangitis obliterans: methods of diagnosis of chronic occlusive arterial lesions distal to the wrist with illustrative cases. *American Journal of the Medical Sciences* 1929; **198:** 237–44.
11. McLeskey CH, Mims GR. Doppler-assisted radial artery cannulation. *Anesthesiology* 1982; **57:** A25.
12. Mozersky DJ, Buckley CJ, Hagood CO Jr, Capps WF Jr, Dannemiller FJ Jr. Ultrasonic evaluation of the palmar circulation. A useful adjunct to radial artery cannulation. *American Journal of Surgery* 1973; **126:** 810–2.
13. Husum B, Palm T. Before cannulation of the radial artery: collateral arterial supply evaluated by strain-gauge plethysmography. *Acta Anaesthesiologica Scandinavica* 1980; **24:** 412–4.
14. Raju R. The pulse oximeter and the collateral circulation. *Anaesthesia* 1986; **41:** 783–4.
15. Bowler GMR, Galloway DW, Meiklejohn BH, MacIntyre CCA. Sharp fall in blood pressure after injection of heparin containing chlorbutol. *Lancet* 1986; **1:** 848–9.

Anaesthesia, 1987, Volume 42, pages 1074–1077

CASE REPORT

Cardiac arrest in near-term pregnancy

S. L. LINDSAY AND G. C. HANSON

Summary

This case study emphasises the multiple factors that may be involved in the precipitation of electromechanical dissociation, which are compounded by additional problems that relate to pregnancy. It reinforces the value of the tracheal route for drug administration when a central vein is not cannulated and stresses the importance of posture and early consideration of Caesarean section in the pre-term gravid patient who has sustained a cardiac arrest.

Key words

Complications; arrest, cardiac.
Pregnancy.

Cardiac arrest is rare in obstetric practice, and this case report highlights several important points with regard to resuscitation in the gravid patient. Towards term, in the supine position the inferior vena cava becomes occluded by the gravid uterus and venous return becomes dependent upon collateral blood flow via the azygos and paraspinal veins.[1] Pressure from the uterus can be minimised by manual displacement or by appropriate positioning of the mother.

The route of administration of drugs during an arrest is important. Kuhn and co-workers[2] showed that dye injected into a peripheral vein during cardiopulmonary resuscitation takes over 300 seconds to reach a central artery, and therefore recommended that drugs should be given via a central vein. It is rare in obstetric practice to have a central line in position at the time of the arrest, and the trachea has been shown to provide a rapid route to the central blood volume.

Case history

An 18-year-old primagravida at 32 weeks' gestation was transferred to the intensive therapy unit from another hospital. She had been found at home in a pool of vomit. Previous antenatal history included an admission at 28 weeks' gestation, with a diastolic arterial pressure of 90 mmHg and albuminuria. She was discharged one day later after no treatment. She had complained of a severe headache and had noted increasing puffiness of her hands and face for 5 days prior to her present admission.

On admission to the accident and emergency department of another hospital, she was unrousable, with grunting respirations and had a dia-

---

S.L. Lindsay, MB, BS, FFARCS, Anaesthetic Registrar, G.C. Hanson, MB, FRCP, Consultant Physician in Charge, ITU, Department of Anaesthesia, Whipps Cross Hospital, Leytonstone, London E11 1NR.

0003–2409/87/101074 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

stolic arterial pressure of 100 mmHg. Ten minutes later, she had a grand mal convulsion which was treated with intravenous diazepam 10 mg and an infusion of chlormethiazole 0.8%. Hypertension was treated with an intravenous infusion of hydralazine 40 mg in 500 ml compound sodium lactate solution.

She was transferred to the labour ward, where her arterial pressure was 180/100 mmHg and heart rate 190 beats/minute. The hypertension persisted because the hydralazine had been accidentally stopped. Practolol 10 mg was given intravenously, which reduced the heart rate to 140 beats/minute, and the systolic pressure decreased to 100 mmHg. An ultrasound examination of the uterus showed no fetal movement. Her trachea was intubated and her lungs ventilated because of her poor condition. Blood gases taken at this stage with $F\mathrm{IO}_2$ 1.0, were pH 7.28, $P\mathrm{aCO}_2$ 4.4 kPa, $P\mathrm{aO}_2$ 6.8 kPa, bicarbonate 17 mmol/litre. The arterial pressure became unrecordable 20 minutes after tracheal intubation. Polygeline 500 ml and 400 ml purified human albumin solution were given with a gradual improvement of the arterial pressure to a value of 130/104 mmHg after 20 minutes.

She was at this time transferred to the intensive therapy unit at this hospital. On arrival she was in a supine position, moribund, with deep central and peripheral cyanosis and cold, mottled peripheries, despite artificial ventilation with $F\mathrm{IO}_2$ 1.0.

The rapid sequence of subsequent events is summarised in Table 1. At time 0 minutes the femoral and carotid pulses were weakly palpable and the heart rate was 150 beats/minute. At 5 minutes the carotid and femoral pulses became impalpable and the electrocardiogram showed a rate of 150 beats/minute, consistent with the diagnosis of electromechanical dissociation. She was turned into the left lateral head-down position and 4 ml normal saline containing 2 mg adrenaline was delivered by a Forrester spray down the tracheal tube. Hand ventilation was continued as before. A right internal jugular venous catheter was inserted and showed the central venous pressure to be 17 cm H_2O at the mid-thoracic point.

Table 1. Cardiac arrest near term. Sequence of events following admission to the intensive therapy unit.

Approximate time (minutes)	Clinical state	Treatment
0	Pulse rate 150 beats/minute Carotid pulse weakly palpable	Intubated Hand ventilation $F\mathrm{IO}_2$ 1.0
5	Pulse rate 150 beats/minute (ECG monitor) Carotid pulse impalpable Electromechanical dissociation	
6		Left lateral head-down position Adrenaline 2 mg down tracheal tube
7	Pulse rate 170 beats/minute Carotid pulsation palpable Right atrial pressure 17 cm H_2O	Right internal jugular line inserted
		Dopamine 200 μg/minute commenced via right internal jugular
8	Systolic pressure 150 mmHg Pulse rate 170 beats/minute	
10	Right atrial pressure 8 cm H_2O	Lower segment Caesarean section
20		Dead baby removed Patient turned on back Ventilation adjusted to maintain $P\mathrm{aO}_2 > 8.0$ kPa, systolic pressure > 100 mmHg
Time (hours)		
1 ↓ 5	Steady improvement in clinical condition Pulse rate decreased to 120 beats/minute Gallop rhythm audible at apex Diffuse crepitations throughout both lung fields consistent with pulmonary aspiration	

At 7 minutes the heart rate was 170 beats/minute and arterial pulses were present. An infusion of dopamine was commenced at a rate of 3 μg/kg/minute via the internal jugular catheter. One minute later her systolic arterial pressure was 140 mmHg and heart rate 170 beats/minute. At 10 minutes a decision to extract the baby by Caesarean section was made; this was performed with an obstetric wedge under the right buttock. A stillborn female infant was delivered. The arterial pressure was well maintained per- and postoperatively. Blood gases taken with $F\text{IO}_2$ 1.0 showed pH 7.26, $P\text{aCO}_2$ 4.5 kPa, $P\text{aO}_2$ 7.0 kPa, bicarbonate 15 mmol/litre, base deficit 11 mmol/litre. Immediately postoperatively the heart rate decreased to 150 beats/minute and a gallop rhythm was audible at the apex. The right atrial pressure was 8 cm H_2O.

A positive end expiratory pressure (PEEP) of 0.2 kPa was introduced in an effort to improve arterial oxygenation, and the blood pressure remained stable. The postoperative chest X ray showed diffuse pulmonary infiltrates maximum on the right side, consistent with aspiration. There was also possible cardiomegaly. The correct position of the internal jugular catheter was confirmed.

The clinical and haemodynamic state improved gradually and, 12 hours after the arrest, the heart rate was 100 beats/minute in sinus rhythm, arterial pressure 100/70 mmHg and arterial blood gases with $F\text{IO}_2$ 0.65 and 0.5 kPa PEEP, were pH 7.40, $P\text{aCO}_2$ 3.8 kPa, $P\text{aO}_2$ 11.2 kPa with a base deficit of 6 mmol/litre.The gallop rhythm was still audible at the apex. The ECG was abnormal; it showed T wave inversion in leads V_1 to V_3 and flattening of T waves V_4 to V_5. A tachycardia of 100–120 beats/minute remained despite heavy sedation and optimal arterial oxygenation and, with the persistent ECG changes, a tentative diagnosis of puerperal cardiomyopathy was made. Diastolic blood pressure was intermittently high and was treated by heavy sedation and analgesia. Urine output remained poor, with evidence of impaired renal function: serum creatinine 175 μmol/litre, urea 10.4 mmol/litre. She was maintained on a strict fluid regimen.

Five days after admission she was weaned off the ventilator and breathed spontaneously via a continuous positive airway pressure system for 5 hours before extubation with good arterial blood gases: pH 7.4, $P\text{aCO}_2$ 4.6 kPa, $P\text{aO}_2$ 15.6 kPa, base deficit +3 mmol/litre. There was no neurological deficit. The abnormalities on the chest X ray showed signs of improvement.

Eight days after admission she was discharged to the general ward, where an echocardiogram performed a day later showed a poorly contracting left ventricle with an ejection fraction of 49%. A repeat echocardiogram 6 days later showed that this had improved to 63%. The left ventricle was noted to be dilated. The tachycardia of 100–120 beats/minute persisted on the ward and then decreased to 90 beats/minute. Sixteen days after admission she was discharged home with a normal mental state and no subjective change in cerebral function.

Discussion

This case report illustrates some of the unique problems that complicate resuscitative efforts in the pregnant patient. In order to abolish aortocaval compression, the patient should be tilted head down and turned into the full lateral position, or the uterus pulled off the inferior vena cava manually or with the use of a firm obstetric wedge placed under one buttock. This patient was transferred between hospitals in the supine position; in the critically ill gravid patient where the haemodynamic state is compromised, transfer should be in the full lateral position preferably with a slight head-down tilt. Effective cardiopulmonary resuscitation is impossible in the full lateral position and thus a compromise has to be made: either the patient is rotated at the waist, with the pelvis tilted and the uterus pulled off the inferior vena cava and the thoracic spine allowed to be flat on the bed, or both the pelvis and the thoracic spine are partly rotated (approximately 30° from the horizontal) and the thoracic spine firmly wedged so that external cardiac massage can be continued with the pressure directed at right-angles to the sternum. Both methods are unsatisfactory.

The cardiac output starts to increase early in pregnancy and reaches its maximum of 49% above the nonpregnant level by the 20th week of gestation. Oxygen consumption increases by approximately 15% above the nonpregnant level. These increases are to accommodate the demands of the fetoplacental unit. Thus it is unlikely that external cardiac massage will provide sufficient flow to allow for these extra demands and, unless the primary cause, for example massive hypovolaemia, can be corrected rapidly, fetal and maternal survival is unlikely.

The majority of case reports that concern cardiac arrest have described saving the fetus in a mother already dead.[3,4] There is one case report where Caesarean section was successful in saving mother and fetus.[5] The decision to perform a Caesarean section in this patient was taken because of the effect of the gravid uterus on venous return and because the heart was seriously compromised in spite of successful resuscitation; the heart rate was 170 beats/minute 3 minutes after adequate restoration of blood pressure.

Thus Caesarean section should be performed in cardiac arrest associated with a preterm pregnancy if resuscitation is unsuccessful after 3 minutes. This should be done with the mother in the left lateral head-down position with the thoracic spine wedged so that external cardiac massage can be continued during delivery. The mother should be turned onto her back as soon as the baby is removed so that more efficient external cardiac massage can be maintained.

Greenberg and colleagues[6] showed that instillation of certain drugs via the tracheal tube was effective in an emergency. Drugs that can be given by this route include adrenaline, lignocaine and atropine; the recommended dosages are 2.0, 200 and 2.0 mg, respectively. The drug is diluted with normal saline to a total volume of 5–10 ml maximum and can be instilled as a fine spray or via a catheter; the lungs are then hyperinflated for 5–10 breaths for dispersal. Extensive pulmonary pathology may affect absorption but it is of interest to note that, in this instance, tracheal adrenaline restored cardiac output within 2 minutes. The decrease in cardiac output which ultimately led to electromechanical dissociation was probably related to a combination of factors. The lungs were noncompliant from extensive pulmonary aspiration. This inevitably increases the intrathoracic pressure and thus decreases the inflow volume to the right heart. Volume may have been sequestered peripherally with the use of hydralazine as a hypotensive agent and fluid may have been lost into the lung interstitium secondary to the pulmonary aspiration. Thus volume top-up appeared helpful when the arterial pressure decreased for the first time. Pulmonary aspiration is complicated by an increase in pulmonary vascular resistance and an increase in pulmonary artery pressure.[7] This, coupled with hypoxia, requires that cardiac work and output increase in order to sustain oxygen supply. In this patient, cardiac output was further compromised by the use of practolol and the presence of a puerperal cardiomyopathy. It seems unlikely that the clinical, electrocardiographic and echocardiographic findings would have persisted weeks after the cardiac arrest had there not been diffuse myocardial pathology prior to the arrest. The dramatic response to adrenaline given via the tracheal tube supports the theory that myocardial failure, as opposed to hypovolaemia, was the major factor that precipitated electromechanical dissociation.

Acknowledgments

We thank Mr R. Baldwin, FRCOG, for permission to report this case. Grateful thanks are due to Mrs J. Snell and Mrs P. Walls for their secretarial assistance.

References

1. Kerr MG, Scott DB, Samuel E. Studies of the inferior vena cava in late pregnancy. *British Medical Journal* 1964; **1:** 532–3.
2. Kuhn GJ, White BC, Swetnam RE, Mumey JF, Rydesky MF, Tintinalli JE, Krome RL, Hoehner PJ. Peripheral vs central circulation times during CPR: a pilot study. *Annals of Emergency Medicine* 1981; **10:** 417–9.
3. Weber CE. Postmortem Cesarean section: review of the literature and case reports. *American Journal of Obstetrics and Gynecology* 1971; **110:** 158–65.
4. Arthur RK. Postmortem Cesarean section. *American Journal of Obstetrics and Gynecology* 1978; **132:** 175–9.
5. DePace NL, Betesh JS, Kotler MN. 'Postmortem' Cesarean section with recovery of both mother and offspring. *Journal of the American Medical Association* 1982; **248:** 971–3.
6. Greenberg MI, Roberts JR, Baskin SI. The use of endotracheal medication in cardiac emergencies. In: Rund DA, Wolcott BW, eds. *Emergency medicine manual 1983.* Norwalk, Connecticut: Appleton-Century-Crofts, 1983: 91–101.
7. Toussaint GPM, Chiu Chu-Jeng, Hampson LG. Experimental aspiration pneumonia: hemodynamics, ventilator and membrane oxygenator support. *Journal of Surgical Research* 1974; **16:** 324–9.

Anaesthesia, 1987, Volume 42, pages 1078–1080

CASE REPORT

Anaphylactoid reactions to prilocaine

K. RUIZ, J. D. STEVENS, J. J. A. TRAIN AND J. WATKINS

Summary

Two cases of severe adverse reaction to prilocaine are presented and the immunological basis of the responses is explored.

Key words

Allergy.
Anaesthetic techniques, regional; intravenous.

Numerous reports of adverse reactions to local anaesthetic agents of an apparently immunological nature are to be found in medical journals.[1–4] Many of these reactions occur on first exposure to the drug, which makes a true immune (antibody mediated) mechanism unlikely in most cases. Type I hypersensitivity reactions to local anaesthetic agents are rare[5] and relatively few adverse reactions are antibody mediated, although they may involve other factors of the immune system.[6] We report one case in the latter category and one as yet unclassifiable, following the use of 0.5% plain prilocaine in Bier's block.

Case histories

Case 1

An 83-year-old woman inpatient presented for open reduction of a repeatedly dislocating proximal interphalangeal joint of the right middle finger. Apart from a history of exertional angina, systematic enquiry was unremarkable and she denied any allergies. Examination revealed a blood pressure of 190/100 mmHg. There was no evidence of Raynaud's disease.

A Bier's block was attempted using a 20-gauge cannula into a vein in the dorsum of the hand. There was no possibility of an intra-arterial injection having occurred. When 10 ml 0.5% plain prilocaine had been injected there was an immediate discoloration of the limb and the patient experienced severe pain. There was some oedema but no urticaria or blistering (Fig. 1). The procedure was abandoned. Twenty minutes elapsed before the cuff was deflated and no untoward systemic reaction occurred. Investigations revealed her IgE level to be <5 IU/ml (normal range 20–70 IU/ml).

Case 2

A 61-year-old woman presented to the accident and emergency department after she had sustained a Colles' fracture of her left wrist. She had received regular thyroxine since a thyroidectomy some 15 years earlier and had no allergies. She had very mild psoriasis for which she took no treatment. Two previous general anaesthetics

---

K. Ruiz, BMedSci, MB, ChB, Senior House Officer, J.D. Stevens, MB, BS, Registrar, J.J.A. Train, MB, ChB, Senior House Officer, Department of Anaesthetics, J. Watkins, BSc, PhD, Deputy Director, Supraregional Protein Reference Unit, Department of Immunology, Royal Hallamshire Hospital, Sheffield S10 2JF.

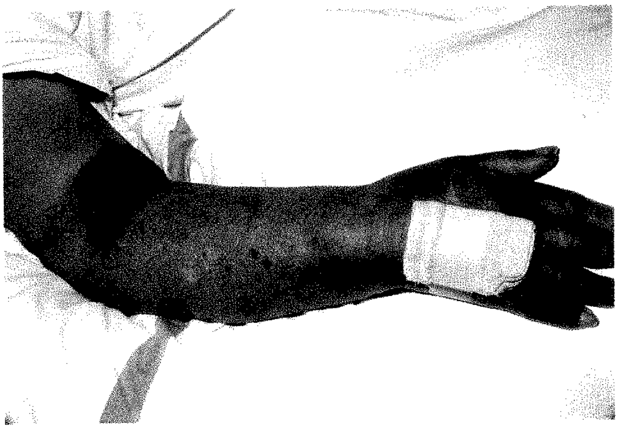


Fig. 1. Note the discoloration of the limb and the sharp cuff demarcation line.

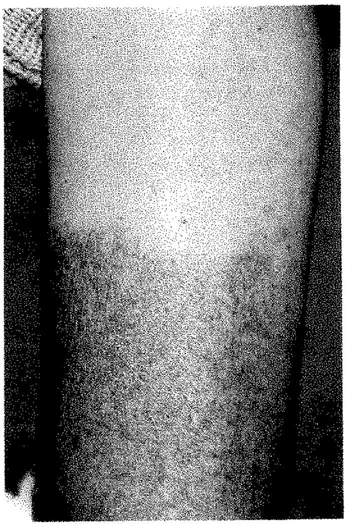


Fig. 2. Note again the discoloration and the clear cuff demarcation line.

were uneventful. Examination was unremarkable and chest X ray and ECG were within normal limits. Raynaud's disease was not present.

A Bier's block using 40 ml 0.5% plain prilocaine was planned. After 5 ml of the solution had been injected into a vein in the dorsum of the hand the arm suddenly became very painful. An acute vasculitic appearance of the limb followed, with no urticaria, blistering or oedema (Fig. 2). There was no possibility of intra-arterial injection. With the cuff left inflated, a general anaesthetic was administered using etomidate 16 mg followed by an oxygen, nitrous oxide, isoflurane mixture. The fracture was reduced and immobilised appropriately.

After recovery from the general anaesthetic (and 30 minutes after the injection of prilocaine), hydrocortisone 100 mg was adminstered intravenously in the unaffected arm prior to cuff deflation. No untoward systemic reaction occurred but the patient was admitted to hospital overnight for observation. The following morning the appearance of the arm remained unchanged but the pain had resolved completely. Subsequent investigation showed slight but probably insignificant elevation of her IgE level, at 100 IU/ml.

Discussion

A hypothesis regarding IgE levels and anaphylactoid reactions has been proposed.[7] This categorises four groups of individuals capable of anaphylactoid responses. These are, firstly, patients with high plasma IgE (> 500 IU/ml) involving classical atopy or allergy, with high binding of IgE to mast cells, predisposing to Type I hypersensitivity reactions; secondly, high circulating IgE (~200–300 IU/ml) but with low affinity for mast cells, which exhibit unprotected surface sites and may 'fire' through physicochemical stimulation: the patient does not exhibit clinical atopy; thirdly, low circulating IgE (< 10 IU/ml) with normal affinity for mast cells but in insufficient amounts to protect the mast cells from direct stimulation: the patient may respond as previously; and fourthly, low circulating IgE (< 10 IU/ml) but with high or normal levels bound to mast cells suggestive of high-affinity antibody. Classical allergy may be exhibited, as in the first possibility.

Our first patient would appear to fit the third category. The second patient appeared normal and may have exhibited a dose-related idiosyncratic response. However, despite her denial of previous exposure to local anaesthetic agents, this may be doubtful and a possibility of an immune response must be considered. It is also possible that the reactions occurred not to prilocaine but to its preservative, methylhydroxybenzoate, and this has been described.[3]

Neither of our patients exhibited a generalised anaphylactoid response because of the cuff employed, central to the Bier's block. Oedema was limited as there was little blood in the limb from which fluid could escape. Any vasoactive substance initially released would have been inactivated by the time the cuffs were deflated. Figures 1 and 2 illustrate the intense and localised nature of the reaction.

Patients with either extremely high or extremely low plasma IgE levels may well be at similar risk of anaphylactoid response, albeit by different mechanisms and to a variety of intravenous drugs. Patients who have previously reacted, and their close family, may be similarly at risk.

Certain recommendations can be made. It would be impractical to assay each patient's IgE level whenever any procedure is contemplated and, in any case, evidence in support of the hypothesis is still far from conclusive. Administration of a test dose of 1–2 ml 0.5% plain prilocaine prior to Bier's block and, with the cuff inflated, waiting 5 minutes before the full dose is given, may be helpful in the avoidance of both genuine immune-mediated reactions and the largely dose-related responses which appear to be associated with low IgE levels. Should such a reaction occur, after the patient has been stabilised thought should be given to taking blood samples for laboratory investigations.[7] At the very least the patient ought to be advised to avoid both the drug and, perhaps, other known histamine-releasing formulations. We would also recommend that this information be kept in writing and carried by the patient at all times, ideally in bracelet or necklace form.

Minimisation of the number of drugs given and, in the case of local anaesthetic agents, avoidance of preparations with preservatives, would appear to be a worthwhile precaution in all anaesthetic techniques.

References

1. Fisher MMcD, Graham R. Adverse responses to local anaesthetics. *Anaesthesia and Intensive Care* 1984; **12:** 325–7.
2. Fisher MMcD, Pennington JC. Allergy to local anaesthesia. *British Journal of Anaesthesia* 1982; **54:** 893–4.
3. Johnson WT, DeStigter T. Hypersensitivity to procaine, tetracaine, mepivacaine and methylparaben: report of a case. *Journal of the American Dental Association* 1983; **106:** 53–6.
4. Seskin L. Anaphylaxis due to local anaesthesia hypersensitivity: report of a case. *Journal of the American Dental Association* 1978; **96:** 841–3.
5. Schatz M. Skin testing and incremental challenge in the evaluation of adverse reactions to local anesthetics. *Journal of Allergy and Clinical Immunology* 1984; **74:** 606–16.
6. Watkins J. Anaphylactoid reactions to I.V. substances. *British Journal of Anaesthesia* 1979; **51:** 51–60.
7. Watkins J, Wild G, Clarke RSJ. Allergy, plasma IgE level and anaphylactoid response: a hypothesis. *Anaesthesia* 1985; **40:** 362–5.

Anaesthesia, 1987, Volume 42, pages 1081–1084

CASE REPORT

A case of prolonged hypotension following intravenous guanethidine block

E. SHARPE, R. MILASZKIEWICZ AND F. CARLI

Summary

A 25-year-old female developed causalgia following a nerve injury in the left hand, and this was treated successfully with a series of intravenous guanethidine blocks. However, after the 13th block, systolic arterial blood pressure decreased to 60 mmHg and remained low (80 mmHg) for one week. Accumulation of guanethidine at the sympathetic nerve ending, resulting in autonomic denervation, might be the underlying mechanism of the prolonged hypotension. Treatment was conservative; however, the use of tricyclic antidepressants and sympathomimetic amines to restore the blood pressure to a normal level can be considered with appropriate caution.

Key words

Anaesthetic techniques; intravenous regional.
Complications; hypotension.

The use of intravenous guanethidine by the Bier technique to treat causalgia of a limb is well documented and used in daily clinical practice. The technique originally described by Hannington-Kiff[1] has been adopted in this centre and repeated blocks are performed on alternate days until complete pain relief is achieved. We report a case of severe and persistent hypotension which occurred after a repeated guanethidine block.

Case history

A 25-year-old female riding instructor was injured in 1983 when she was stabbed through her left thenar eminence with a pitchfork, which resulted in damage to the digital nerves of her left thumb. She underwent surgical exploration and repair at her local hospital. Subsequently she developed severe hyperpathia over the radial and ulnar aspect of the left thumb and palm. She was treated by physiotherapy and splintage but mild analgesics failed to relieve her pain.

She was referred to this centre for investigation and treatment one year after the initial injury. On examination, her thumb was adducted at the metacarpophalangeal joint and flexed at the interphalangeal joint in a protective manner. No wasting of the thenar muscles was present but thumb movements were impaired as a result of

---

E. Sharpe, MB, BS, Senior House Officer in Rheumatology and Rehabilitation, R. Milaszkiewicz, MB, BS, Registrar, F. Carli, FFARCS, Senior Registrar, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, Middlesex.

Correspondence should be addressed to Dr F. Carli, Department of Anaesthesia, Northwick Park Hospital and Clinical Research Centre, Watford Road, Harrow, Middx.

0003–2409/87/101081 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

the hyperpathia. An electromyogram showed no abnormality of motor conduction. A diagnosis of causalgia was made.

She was admitted to hospital for a programme of intensive rehabilitation and intravenous regional guanethidine blocks. These are routinely performed on alternate days by a physician. Following exsanguination of the arm and with the tourniquet inflated to 300 mmHg, guanethidine 10 mg in 20 ml saline together with 5 ml 1% lignocaine were injected via an indwelling needle into a vein close to the area of hyperpathia. The tourniquet was left inflated for 20 minutes and then slowly deflated. Vital signs were measured every 15 minutes for 4 hours while the patient remained supine. No sedation was used during the procedure so that the patient could cooperate with the physiotherapist as soon as possible after performance of the block.

The hyperpathia started to disappear following the first four blocks, with improved movement of the left hand. While the third block was performed, 10 mg of guanethidine accidentally entered the systemic circulation while the cuff was not inflated. A transient period of hypotension (systolic arterial pressure 90 mmHg) followed, without any further side effects.

A total of 13 guanethidine blocks were administered successfully over the period of 5 weeks and the patient was able to move the hand freely without pain. However, she complained of increasing tiredness over this period of time. Following the 13th block, her systolic arterial blood pressure remained low (80 mmHg) for 2 hours and then decreased to 60 mmHg, with a pulse rate of 36 beats/minute. She became drowsy, pale and was sweating with peri-orbital oedema. She was transferred from the rehabilitation ward to the intensive care unit for observation and monitoring of her cardiovascular status. Atropine and glycopyrronium were administered intravenously and a transient increase in heart rate and arterial pressure were observed for one hour. A fluid challenge of 300 ml of normal saline had no effect on the arterial pressure, which remained at 60 mmHg for 10 hours. However, urine output was satisfactory and her skin was warm and well perfused. Systolic arterial pressure and pulse rate remained at 80 mmHg and 40 beats/minute respectively for one week, during which time she received treatment for her headache and blurred vision with mild analgesics. She remained anorexic and fluids were administered intravenously for one week.

Nine days later the patient became mobile and, despite her continuous tiredness, no orthostatic hypotension was noted. She was discharged from the hospital 21 days later, when she still felt tired. She was seen 3 months later in the outpatient department and, in response to exercise, the systolic arterial pressure increased from 105 to 120 mmHg and the pulse rate from 75 to 135 beats/minute. She was by then back to full work but still complained of tiredness during the day, sufficient to necessitate an afternoon rest.

Discussion

Since the original description of the intravenous regional sympathetic block with guanethidine in 1974,[1] this technique has found application in several clinical situations such as causalgia, reflex sympathetic dystrophies,[2,3] Raynaud's disease and, more recently, in vascular surgery of the limb[4] and limb angiography.[5] Guanethidine is an adrenergic neurone blocking agent at the presynaptic site and acts by displacement of noradrenaline from its storage sites in the sympathetic nerve ending.[6] Its subsequent accumulation at this site prevents the re-uptake of noradrenaline and thus results in a prolonged sympathetic blockade. Its accumulation is therefore essential for its action.

These pharmacological characteristics of guanethidine led Hannington-Kiff[1] to adapt the technique described by Bier in 1908[7] and infuse 10–20 mg guanethidine into the affected limb. He recommended the tourniquet be kept inflated for at least 10 minutes for the drug to be fixed in the tissues so that, on release of the tourniquet, little guanethidine would escape into the general circulation.

The mechanism of causalgia is thought to be related to a breakdown of insulation between sympathetic and sensory nerves at the site of partial nerve damage; this forms an electrical synapse (ephapse) which results in pain in the affected area.[8] This view (ephaptic conduction hypothesis) has recently been challenged by some workers, who suggest that a hypersensitivity to noradrenaline might be the underlying mechanism.[9,10] However, there is growing evidence that cross talk exists between abnormal demyelinated nerve fibres at any site of a peripheral nerve. Peripheral sprouts are potent causes of spontaneous discharges and these sprouts may grow backwards along a considerable length of the nerve and thus act as sites for ephaptic discharges.[11]

Any peripheral nerve damage, however slight, produces central effects in the spinal cord; these include spontaneous firing of de-afferented neurones, sprouting with inappropriate connexions as the source of abnormal discharges, and the unmasking of de-afferented cells. The understanding of these mechanisms has led to a much more logical approach to treatment. Repeated sympathetic blocks, achieved most successfully with guanethidine, exhaust the peripheral receptors of noradrenaline and thus abolish the sensitivity of the 1A afferents to circulating noradrenaline and allow more normal movement patterns to be established.[12] Serial guanethidine blocks instead of a single block were started in this centre between 1980 and 1982 and this has certainly improved the success rate.[13]

No serious side effects following guanethidine block have been reported except for mild orthostatic hypotension which can occur as a result of either a residual effect of guanethidine released from the limb, or an increased circulatory capacity.[14] We are not aware of any persistent hypotensive episode that has occurred after single or repeated guanethidine blocks, as happened in this case. We do not have an explanation for this phenomenon; however, it has been reported that chronic administration of guanethidine in hypertensive patients produces a supersensitivity of effector cells that is very similar to that due to sympathetic post-ganglionic denervation. It is greater for noradrenaline than for adrenaline and can be explained by a chronic absence of released mediator.[15] It might, therefore, be possible that either the accidental intravenous injection of 10 mg of guanethidine while the third block was performed, or an accumulation of the small amounts of guanethidine released in the circulation after each block, together with a supersensitivity at the ganglion site, might have caused a prolonged hypotensive episode. The increasing tiredness complained of by the patient might have been a warning sign. However, this symptom is so common following either guanethidine block for causalgia or administration of guanethidine for the treatment of hypertension, that it cannot be relied upon.

The treatment carried out in this case was conservative and aimed at maintenance of an adequate perfusion pressure to the major organs. The use of tricyclic antidepressants to antagonise the effect of guanethidine was suggested by Mitchell and Oates[16] but it proved ineffective in acute situations, like the present, where there was a need to restore a satisfactory perfusion pressure to the major organs. Furthermore, an indirect increase of catecholamines following the administration of tricyclics, might have produced untoward effects since guanethidine *per se* would cause an acute increase in the sensitivity to noradrenaline and adrenaline. Administration of sympathomimetic amines which inhibit the uptake and subsequently the action of guanethidine has also been considered. However, one has to be reminded that the concentration of catecholamines in the adrenal medulla is not lowered by guanethidine, and responses that involve the release of amines from this site might be unpredictable.

In conclusion, guanethidine block therapy is used widely in our centre for the relief of causalgia and has improved our success rate, but careful monitoring of the cardiovascular system is important to prevent what could be a disaster in otherwise healthy patients.

Acknowledgments

The authors wish to thank Dr C.B. Wynn Parry for his suggestions and criticism and K. Lewis for typing the manuscript.

References

1. HANNINGTON-KIFF JG. Intravenous regional sympathetic block with guanethidine. *Lancet* 1974; **1:** 1019–20.
2. LOH L, NATHAN PW. Painful peripheral states and sympathetic blocks. *Journal of Neurology, Neurosurgery and Psychiatry* 1978; **41:** 664–71.
3. TAKESHI T, SHIBASAKI H, KUROIWA Y. Reflex sympathetic dystrophy (causalgia) treatment with guanethidine. *Archives of Neurology* 1983; **40:** 430–2.
4. DAVIES KH. Guanethidine sympathetic blockade: its value in reimplantation surgery. *British Medical Journal* 1976; **1:** 876–7.
5. VAUGHAN RS, LAWRIE BW, SYKES PJ. Use of intravenous regional sympathetic block in upper limb angiography. *Annals of the Royal College of Surgeons* 1985; **67:** 309–12.
6. GOODMAN LS, GILMAN A. *The pharamacological basis of therapeutics*, 7th edn. New York: MacMillan, 1985: 204–6.

7. Bier A. Ueber einen neuen Weg Localanasthesie an den Gliedmaassen zu erzeugen. *Archiv fur klinische Chirurgie* 1908; **86:** 1007–10.
8. Wall PD, Gutnick M. Properties of afferent nerve impulses originating from a neuroma. *Nature* 1974; **248:** 740–3.
9. Ochoa JL, Torebjork HE. Paraesthesiae from ectopic impulse generation in human sensory nerves. *Brain* 1980; **103:** 835–53.
10. Wallin G, Torebjork HE, Hallin R. Preliminary observations on the pathophysiology of hyperalgesia in the causalgic pain syndrome. In: Zotterman Y, ed. *Sensory function of the skin in primates*. Oxford: Pergamon Press, 1976: 489–502.
11. Scadding JW. Peripheral neuropathies. *Postgraduate Medical Journal* 1984; **60:** 413–25.
12. Wynn Parry CB, Withrington RH. Painful disorders of peripheral nerves. *Postgraduate Medical Journal* 1984; **60:** 869–75.
13. Withrington RH, Wynn Parry CB. The management of painful peripheral nerve disorders. *Journal of Hand Surgery* 1984; **9:** 24–8.
14. Thomsen MB, Bengtsson M, Lassvik C, Lewis DH, Elfstrom J. Changes in human forearm blood flow after intravenous regional sympathetic blockade with guanethidine. *Acta Chirurgica Scandinavica* 1982; **148:** 657–61.
15. Sannerstedt R, Conway J. Hemodynamic and vascular responses to antihypertensive treatment with adrenergic blocking agent: a review. *American Heart Journal* 1970; **79:** 122–7.
16. Mitchell JR, Oates JA. Guanethidine and related agents. I. Mechanism of the selective blockade of adrenergic neurons and its antagonism by drugs. *Journal of Pharmacology and Experimental Therapeutics* 1970; **172:** 100–7.

Anaesthesia, 1987, Volume 42, pages 1085–1091

APPARATUS

Closed-loop administration of atracurium

Steady-state neuromuscular blockade during surgery using a computer controlled closed-loop atracurium infusion

N. R. WEBSTER AND A. T. COHEN

Summary

The advent of newer muscle relaxants with predictable rates of metabolism and times of offset of neuromuscular blockade now makes it possible to use intravenous infusion safely as a mode of delivery. This has many advantages over administration by intermittent bolus. Moreover, it is feasible to use a servo system for their delivery. We have developed and evaluated such a system which is portable and requires little computer expertise to set up and use. It is a useful adjunct to routine anaesthesia, as well as a potentially powerful research tool.

Key words

Anaesthetic techniques; infusion.
Neuromuscular relaxants; atracurium.

Closed-loop or servo mechanisms have been used for many years in the engineering field in the control of heating systems. An automatic control system of this type functions by constant or intermittent comparison of its output with its input through feedback, so that the error or difference between the two quantities can be used to bring about the desired amount of control. With recent advances in electronic hardware there has been an increasing awareness of their potential for use in the clinical environment. For example, arterial blood pressure, intracranial pressure, plasma glucose concentration, neuromuscular blockade as well as the delivery of volatile anaesthetics, are all variables which are readily controlled by computer.[1–4]

With improvements in monitoring, considerably more information is made available to the anaesthetist. However, there is a limit to the quantity of data that can be absorbed and acted upon at any one time. We consider it important for systems to be developed that will aid in the interpretation and subsequent application of this information. Closed-loop control systems have the dual function of both monitoring a variable as well as maintaining it within a previously defined range. Technical advances can be used which extend the capabilities and, in particular, increase the speed of response of the anaesthetist to changes in various measured parameters. However, he or she must be aware of the limitations of this form of simple control system.

An ideal control system for use in the clinical environment should be compact and portable, inexpensive and easy to operate. It should be based on a stable negative-feedback loop with time constants and damping characteristics

---

N.R. Webster, BSc, MB, ChB, PhD, FFARCS, Honorary Consultant, Clinical Research Centre, Division of Anaesthesia, Watford Road, Harrow, Middlesex HA1 3UJ, A.T. Cohen, MB, ChB, DRCOG, FFARCS, Consultant, Department of Anaesthesia, St James's University Hospital, Beckett Street, Leeds LS9 2TF.

0003–2409/87/101085 + 07 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

consistent with minimal overshoot and undershoot. To achieve and maintain a steady state rapidly the system should have a minimum number of time lags, each of minimum duration. This stability should be maintained over a wide range of operating states short of catastrophic failure.

Muscle relaxants have traditionally been administered by bolus injection with scant regard to their pharmacokinetics, at time intervals determined by the anaesthetists' clinical experience or by patient movement. If the duration of surgery is misjudged the patient may remain paralysed for some time at the end. With the advent of muscle relaxants with short half-lives it is now possible accurately to control the state of relaxation throughout surgery and at a level that is compatible with rapid reversal if required. The most appropriate method of administration to achieve this is by continuous infusion but it is important to monitor accurately the degree of neuromuscular block in order to avoid over or under dosage.

However, systems developed to date have used equipment more commonly seen in laboratories and involve complex computer and infusion equipment unsuitable for use by the clinical anaesthetist. Therefore, we have developed an automatic system for the intra-operative control of muscle relaxation during routine anaesthesia which we have evaluated under a variety of clinical conditions.

Methods

Sensor

Currently two methods of measurement of evoked muscle response are in use: assessment of the evoked muscle tension using a force transducer, or mechanomyography; and measurement of the evoked muscle action potential, or electromyography (EMG). In each case the response to various patterns of nerve stimulus may be estimated, i.e. single, train-of-four (TOF) or tetanic stimulation.

The use of a force transducer has, until recently, been the only practical technique available to the anaesthetist. It is difficult and time consuming to set up and prone to errors related to transducer movement. The Datex neuromuscular transmission monitor (NMT100) has been advocated as an easy to use and reliable monitor which provides a clinically useful measurement of neuromuscular function,[5] and was used throughout.

Five ECG-type silver/silver chloride electrodes (Datex disposable surface electrodes) were applied: two stimulating electrodes over the ulnar nerve in the forearm, a ground electrode at the wrist and two recording electrodes placed over the hypothenar muscles. The stimulator produces a train of four stimuli, of pulse width 100 μs and frequency 2 Hz, every 20 seconds. Stimulus current is 0–70 mA; the supramaximal stimulus current (20% above maximal current) is determined automatically.

The EMG response was assessed from the two surface electrodes over the hypothenar muscles via a fully isolated differential pre-amplifier. The stimulus from the NMT100 automatically triggers the EMG response processor to commence operation. In normal measurement this results in the gate which accepts response information being opened 3 ms after the stimulus and kept open for 10 ms; the area within the compound action potential is rectified and then integrated. This gating reduces stimulus artifact. The NMT100 was equipped with revision 11 software which provides an indication of stimulus artefact. With correct electrode placement the recorded stimulus artefact was less than 10% in all cases. The device calculates and displays T1% and TR% values, where T1% is the height of the first twitch as a percentage of control and TR% is the fourth twitch as a percentage of the first (TOF ratio). A 15-minute memory facility on loss of mains power enables the patient to be transferred into the operating theatre and the computer controlled infusion equipment to be set up without loss of the control value.

A serial (RS232C; 300 baud, 8 bit, 1 stop bit, no parity) computer output is provided via a 9-pin D connector at the back of the NMT100. Data output is in the form of a string of characters which consist of the EMG response to all four twitches, the control EMG value and error codes; this enables T1% and TR% to be calculated.

Processor

Any computer with programmable serial input/output facilities and sufficient memory to hold a 16K program can be used in this system. The authors chose a battery-operated portable computer with liquid crystal display and non-volatile random access memory (RAM). The system has been used successfully with two such computers (Tandy 100, Epson HX-20).

Software

There are three commonly used components to a control system and these can be defined simply as follows: proportional, controller gain uniformly proportional to input; integral, response to an error signal increases as long as error is present (this eliminates steady-state offset); and derivative, anticipates the trend of the error signal and applies a correcting action ahead of this error: this reduces the time to achieve the desired steady-state value. These components can be represented as mathematical equations (see Appendix).

A proportional and derivative controller algorithm written in Microsoft Basic and using 4K of memory, directs the computer to receive a signal from the NMT100 every 20 seconds and updates the infusion rate each minute. The controller has been designed to achieve a set point of T1% = 10 and not to exceed an acceptable clinical range of 5–15. Knowledge of the response times of the total system and the drug in isolation was required to optimise the algorithm and such details could be obtained only by field testing the equipment in the operating theatre. The output to control the infusion device is in the form of a serial signal of a single 8-bit ASCII code transmitted via the same serial port as the input. Figure 1 is a flow chart that details the functioning of the controller. The software permits the computer intermittently to save the infusion rate and T1% in memory, for later analysis. By the end of the study software had been written which supported the use of the microcassette in the HX-20 as a data logger. This stores every data point and enables subsequent graphs of infusion rate against time to be produced, such as Figs 2 and 3.

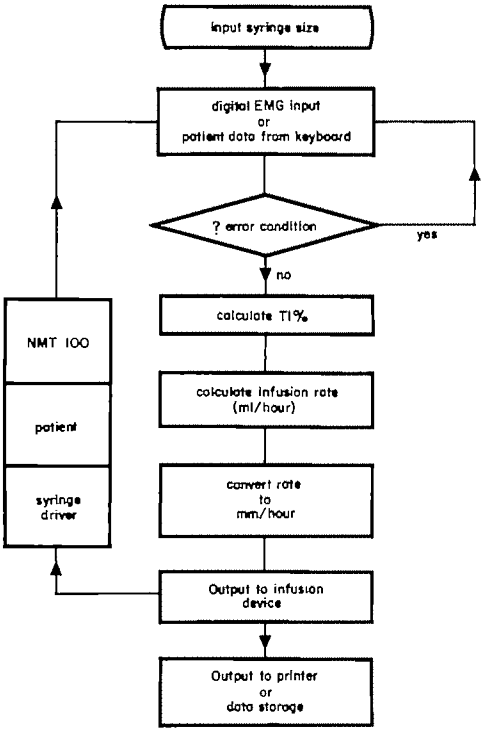


Fig. 1. Flow chart detailing function of controller.

Delivery system

A Graseby MS16A syringe driver modified for computer control was used.[6] This is an inexpensive, portable, battery-operated syringe driver of the type used by diabetics for the infusion of insulin and by ambulatory patients for the relief of chronic pain. A 5- or 10-ml syringe that contained atracurium (10 mg/ml) was fixed to the pump and connected to the patients when they entered the operating theatre.

Evaluation

The ability of the system to achieve steady state at predicted relaxant infusion rates was confirmed by use of a second microcomputer programmed to simulate the output of the NMT100 during anaesthesia. Further evaluation of the system to establish the response times of its components and to confirm the simulated results, required clinical testing. During the evaluation period the system was used on patients on routine operating lists. Any patient in whom muscle relaxation was anticipated for a period greater than 45 minutes was considered suitable for inclusion in the study.

All patients were premedicated with oral diazepam 5 or 10 mg 1–2 hours pre-operatively as appropriate. On arrival in the anaesthetic room the NMT100 electrodes were sited and dedicated venous access established. Anaesthesia was induced with sodium thiopentone 4 mg/kg. Once a control reading on the NMT100 was

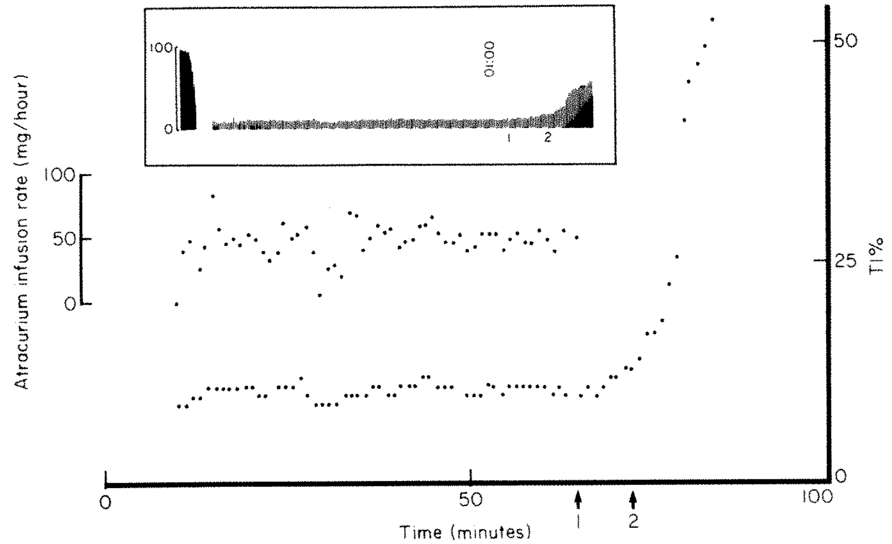


Fig. 2. Graph of muscle relaxation (T1%) and atracurium infusion rate against time. A bolus of atracurium 0.5 mg/kg was administered at induction of anaesthesia (time 0). T1% never decreased to 0. The tracings commence as the system comes under computer control. Marker 1, cessation of atracurium infusion; marker 2, reversal of neuromuscular blockade. The corresponding NMT100 trace is shown in the inset.

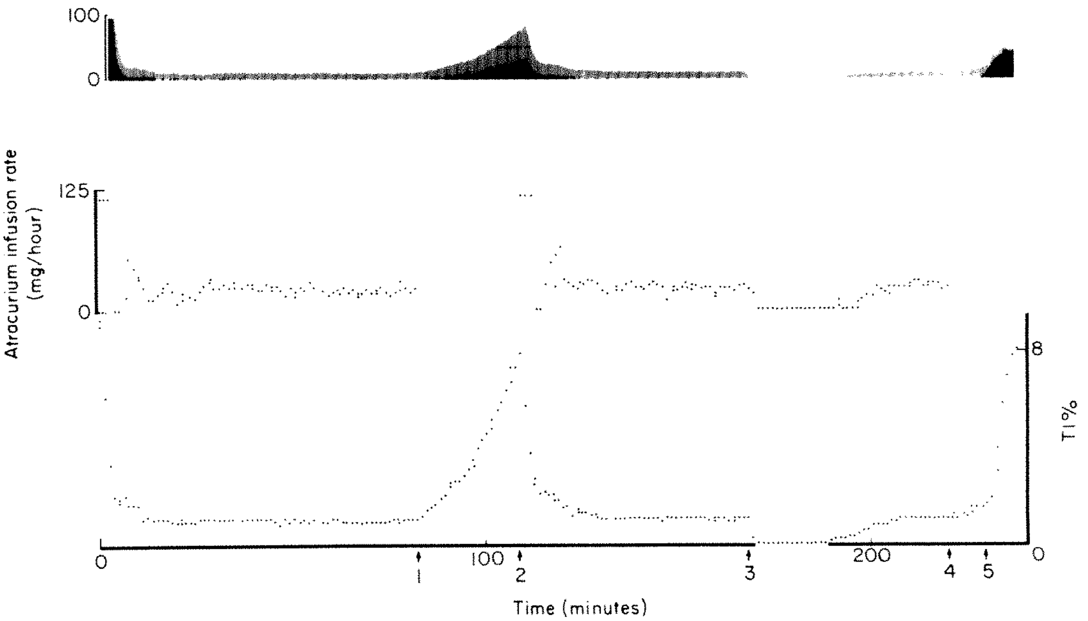


Fig. 3. Further graph of muscle relaxation (T1%) and atracurium infusion rate against time. In this study the patient was connected directly to the system without a prior bolus of relaxant. The effects of two intentional disturbances can be seen. Marker 1, atracurium infusion disconnected from the patient and T1% allowed to rise; marker 2, infusion reconnected. A rapid response and lack of overshoot is demonstrated. Marker 3, bolus dose of atracurium (7.5 mg) administered. This results in a rapid increase in neuromuscular block followed by a slow return of function and a corresponding slow increase in atracurium infusion rate. Markers 4 and 5, end of infusion and reversal of neuromuscular blockade, respectively. These traces demonstrate the performance characteristics of the system, in particular the short lag and response times and the overall stability. The corresponding NMT100 trace is shown at the top of the figure.

Table 1. Patient demographic data and details of surgery and duration of anaesthesia (induction of anaesthesia to reversal of neuromuscular blockade).

Age (years)	Sex	Weight (kg)	ASA grade	Procedure	Time (minutes)
50	M	58.4	2	Gastro-oesophagectomy	266
63	M	75.0	2	Hernia repair	55
44	F	69.0	1	Varicose veins	41
1	M	10.7	1	Rectosigmoidectomy	199
13	M	46.3	1	Bat ears	80
3	M	15.2	1	Hypospadias repair	237
4	M	17.0	1	Anteromedial release	60
5	M	22.5	1	Dermoid excision	53
37	F	80.0	1	Mastoid exploration	153
33	F	90.0	4	Phaeochromocytoma	137
1	M	8.9	1	Imperforate anus	135
3	M	15.0	1	Hypospadias repair	69
1	F	10.6	1	Closure of colostomy	70
3	M	14.0	1	Hypospadias repair	100
2	M	20.0	1	Hypospadias repair	70
11	M	58.2	1	Bilateral orchidopexy	65
3	M	14.3	1	Laparoscopy/orchidopexy	114
14	M	51.0	1	Orchidopexy	75
19	M	60.0	1	Correction pectus excavatum	125
73	M	80.0	3	Gastro-oesophagectomy	310

Table 2. Neuromuscular function and infusion details. Time to reversal is measured from injection of atropine and neostigmine.

Infusion details	Mean	SEM
T1% (steady state)	8.90	0.47
Infusion rate at steady state (mg/kg/hour)	0.45	0.02
Time to reach steady state from computer switch-on (minutes)	13.57	1.12
Time to reversal (minutes)	2.65	0.35

obtained the patient was paralysed with atracurium 0.5 mg/kg and a tracheal tube passed. Anaesthesia was maintained by ventilation with nitrous oxide 70% in oxygen and enflurane 0.5%; supplements of fentanyl 2 μg/kg were administered as appropriate. After the patient and the NMT100 were transferred to the operating theatre the computer controlled pump, charged with a syringe of undiluted atracurium 10 mg/ml, was connected to the patient and the NMT100 linked to the computer input–output port. The system then took control of neuromuscular blockade.

The infusion was stopped at closure of the peritoneum or an estimated 15 minutes before the end of surgery. Residual neuromuscular blockade was reversed with atropine 40 μg/kg to a maximum of 1.2 mg and neostigmine 80 μg/kg to a maximum of 2.5 mg as the last stitch was placed in the skin. The following times were recorded: bolus injection; end of infusion; atropine and neostigmine administration; return of spontaneous ventilation; and lifting of head.

Results

Twenty patients were studied; patient details can be found in Table 1. Satisfactory muscle relaxation was maintained throughout the surgical procedure in all cases (Table 2). The traces obtained were remarkably stable, with minimal variation in T1% at the steady-state value. Clinically satisfactory reversal as judged by ability to protrude the tongue on command and sustain head lift, was complete by 3 minutes in all cases irrespective of the duration of the infusion.

Figure 2 shows an NMT record obtained from an 84-kg male which demonstrates a rapid onset of muscle relaxation after the initial control value of T1% was established. This is followed by a short break in the trace when the patient was transferred from the anaesthetic room to the operating theatre. This trace is unusual in that 0.5 mg/kg did not result in a T1% of less than 10 after induction. A slightly variable degree of neuromuscular block, associated with a more variable infusion rate, is noted during the course of the infusion, which lasted some 55 minutes (mean infusion rate 53.4 mg/hour, coefficient of variation 23.7%). At no stage did T1% become less than 10 or exceed 13, and the majority (93%) of the readings were less than 13 (mean 11.5, coefficient of variation 6.85%).

Figure 3 shows the effects on the system of two separate intentional disturbances of the steady state. The record was obtained in a 40-kg male patient who underwent prolonged peripheral surgery which did not require neuromuscular blockade. This patient was not given a bolus of atracurium but was connected directly to the controller. These traces demonstrate lag and response times. In both situations (at time zero and mark 2) the infusion was commenced with a T1% greater than steady state and a response occurred within one minute. The response times were variable; T1% decreased from 98 to 15 in 11 minutes at the start of the infusion and from 83 to 15 in 12 minutes later in the infusion. The traces also demonstrate the effect on the steady state, of administration of a 7.5-mg bolus of atracurium at mark 3. The return of muscle tone is accompanied by recommencement of the atracurium infusion with no evidence of overshoot or undershoot in this or any other part of the trace. When the error in T1% was high the T1% trace settled down within 10 minutes although the infusion rate took a little longer, since there is a tendency for oscillation. Once the system had been fully debugged it was found to be easy to use and did not interfere with routine clinical practice.

Discussion

We have developed a portable system which is easy to set up and use in the clinical environment. The automatic and near-optimal control of neuromuscular block simplifies the management of anaesthesia especially during longer cases. We consider this system to be a valuable addition to the equipment at the disposal of the anaesthetist.

Other workers have described closed-loop administration of muscle relaxant with a non-portable mains-powered microcomputer which required a mass storage device and visual display unit.[7,8] They used a purpose-built neuromuscular monitoring system based on a force transducer and constructed a syringe driver controlled by a machine code routine to deliver relaxants by intermittent bolus. For a system to be safe and practical for use routinely in the operating theatre it is important that there is a minimum number of components and interconnexions. In addition, programming techniques should permit easy software updating and modification for use with new drugs.

Monitoring of neuromuscular function is beneficial to the anaesthetic management of patients. The properties of the ideal relaxant were summarised previously by Jones[9] as follows: rapid onset of action; prompt and reliable reversal; no tendency to recurarisation; cardiovascular stability; minimal cumulation; and safety in the presence of renal or hepatic dysfunction. After consideration of these ideal features it was felt that atracurium was suitable for study in the present system. Our results confirm ease of reversal and constancy of infusion rate even for prolonged infusions, which indicates minimal cumulation.

Control of neuromuscular blockade in these patients consists merely of a single bolus of relaxant at induction followed by regular refilling of the infusion pump syringe (approximately 2 hourly). The computer controlled loop takes over immediately after the induction bolus of relaxant and is able to maintain the desired level of relaxation until switch-off. For a short time after induction the degree of muscle relaxation was usually less than T1% = 10, due to the bolus effect. However, once stability was achieved, it remained at this level constantly for as long as required (over 5 hours in one case in the present series). Prompt and complete relaxant reversal was found clinically in all cases, even though there was frequently no more than one twitch prior to the injection of neostigmine.

There are several potential problems associated with the use of this system. Firstly, each component is battery powered to maintain portability and avoid potential mains electrical hazards. The low power consumption of the Graseby syringe driver makes battery failure an unlikely problem but failure was experienced once during the development phase and we now replace the battery every 3 months. The interface and computers are equipped with low-battery warning devices and are able to run from a 5 V power source if required.

Secondly, the correct functioning of the NMT100 is dependent on accurate electrode placement (in particular, the positioning of the earth electrode between the stimulating and sensing electrodes appears to be critical) and good electrode contact maintained throughout. Anything that tends to interfere with this good contact, such as pulling leads, excessive sweating or the use of unsatisfactory electrodes, will cause the NMT100 to malfunction.

Thirdly, interference with the delivery of relaxant to the patient due to blockage of the infusion or emptying of the syringe will destabilise automatic control. However, such problems will be readily apparent due to the automatic switch-off alarm of the syringe driver, as well as the alarm functions of the NMT100.

Finally, interference has been noted with some types of diathermy, which causes the NMT100 to display the message 'electrodes off' and indicate a T1% of 0. However, the data stream transmitted at this time will contain an error code which enables the software to be designed to ignore such isolated occurrences and permits distinction from a true 'electrodes off' situation.

This controller was designed for use with an average patient; factors that significantly affect the pharmacodynamic response may lead to instability which results in oscillation of T1%. A system has been described which uses an adaptive tuner to overcome these potential problems.[10]

We have demonstrated that it is possible to design a working system although there are areas suitable for future development. The present system comprises a number of components which could optimally be reduced to a minimum of two—a mains-powered monitor and controller, and a battery-powered syringe driver. This would increase both compactness and portability as well as minimise the number of interconnecting cables. It may be possible to use a remote control system based on infrared, ultrasonic or radio signals to eliminate cables; this would make feasible the control of more than one syringe driver from the same computer.

Appendix

A mathematical representation of the three controller models is given below:

proportional: $m(t) = K_p e(t)$

integral: $m(t) = \int_0^t K_i e(t)\,dt$

derivative: $m(t) = K_d . de/dt$

where $m(t)$ is the actuating (or controller output) signal, $e(t)$ the error signal, K_p the proportional rate constant, K_i the integral rate constant and K_d the derivative rate constant.

References

1. Sheppard LC. Computer control of blood and drug infusions in patients following cardiac surgery. *Journal of Biomedical Engineering* 1980; **2:** 83–4.
2. Smith NT, Quinn ML, Flick J, Fukui Y, Fleming R, Coles JR. Automatic control in anesthesia: a comparison in performance between the anesthetist and the machine. *Anesthesia and Analgesia* 1984; **63:** 715–22.
3. Meline LJ, Westenskow DR, Pace NL. Computer versus anesthesiologist controlled hypotension using sodium nitroprusside. *Anesthesiology* 1985; **63:** A194.
4. Brown BH, Asbury AJ, Linkens DA, Perks R, Anthony M. Closed-loop control of muscle relaxation during surgery. *Clinical Physics and Physiological Measurement* 1980; **1:** 203–10.
5. Pugh ND, Kay B, Healy TEJ. Electromyography in anaesthesia. A comparison between two methods. *Anaesthesia* 1984; **39:** 574–7.
6. Cohen AT. A computer-controlled syringe driver for use during anaesthesia. A modification of the Graseby MS16A. *British Journal of Anaesthesia* 1986; **58:** 670–5.
7. Bradlow HS, Uys PC, Rametti LB. On-line control of atracurium induced muscle relaxation. *Journal of Biomedical Engineering* 1986; **8:** 72–5.
8. Bradlow HS, Rametti LB, Uys PC, Coetzee WP. Microcomputer-based muscle relaxation monitor and controller for clinical use. *Medical and Biological Engineering and Computing* 1985; **23:** 547–55.
9. Jones RM. Neuromuscular transmission and its blockade. Pharmacology, monitoring and physiology updated. *Anaesthesia* 1985; **40:** 964–76.
10. Linkens DA, Menad M, Asbury AJ. Smith predictor and self-tuning control of muscle-relaxant drug administration. *Institute of Electrical Engineers Proceedings, Part D* 1985; **132:** 212–8.

Anaesthesia, 1987, Volume 42, pages 1092–1095

APPARATUS

Monitoring neuromuscular blockade

The table knife transducer

C. R. DUNDAS, I. D. LEVACK AND M. S. BROCKWAY

Summary

A simple and inexpensive force transducer made from a stainless steel table knife is described. Construction is straightforward and utilises strain gauges that are readily available. Amongst its attributes are lightness, ease of application, low sensitivity to postural changes and linearity over extended periods of time.

Key words

Measurement techniques.
Neuromuscular blockade.

The new generation of neuromuscular blocking drugs has generated a widened interest in the monitoring of neuromuscular blockade. Electrical stimulation of a motor nerve and measurement of the resultant isometric tension in the appropriate muscles is a familiar technique. It has been found considerably less subject to interference than the alternative of electromyography.[1] The thumb is almost invariably utilised for monitoring because of its accessibility during surgical procedures and because of the convenient anatomy of adductor pollicis. As this is the only muscle of the thenar eminence supplied by the ulnar nerve, ulnar nerve stimulation results in adduction of the thumb. Many authors have described techniques for the measurement of this adductive force.

Methods that require immobilisation of the arm in a back slab or similar board on which the transducer is attached[2–4] appear to be the least satisfactory, since it is impossible to prevent relative movement between board and arm, which results in baseline instability. The best methods allow direct attachment of the transducer to the hand;[5–7] however, these can prove very expensive because they incorporate commercial transducers.[5,8] The table knife transducer described here is attached directly to the hand, is inexpensive to construct and, to date, has proved very reliable.

Methods

The stainless steel knife is forged into the shape illustrated in Fig. 1. The handle is intended to lie in the palm across the metacarpal heads and be held by the clenched fingers. A bend curves over the head of the second metacarpal and serves to prevent the device being dislodged by adduction of the thumb. The blade of the knife is then curved upwards in the opposite direction and, towards the tip, is shaped to form a shallow

---

C.R. Dundas, FFARCS, FRCP(Glas), Senior Lecturer, Department of Anaesthesia, University of Aberdeen, Foresterhill, Aberdeen, I.D. Levack, MD, FFARCS, Consultant, M.S. Brockway, MB, ChB, Registrar, Department of Anaesthesia, Aberdeen Royal Infirmary, Aberdeen.

0003–2409/87/101092 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

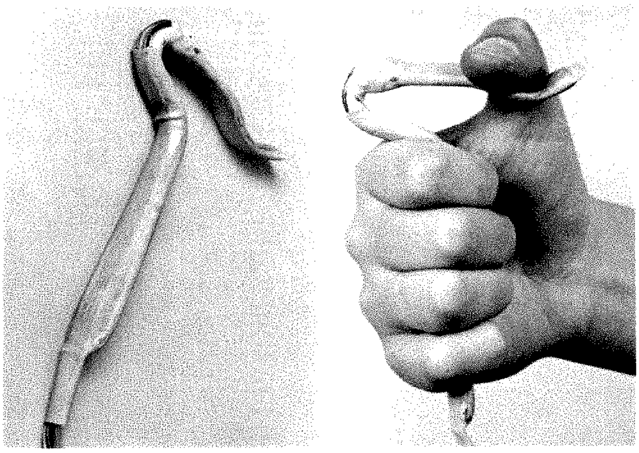


Fig. 1. Stainless steel table knife forged into the shape of the transducer and its position in the hand.

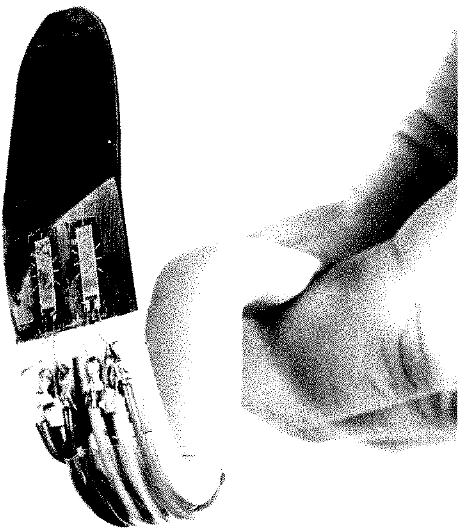


Fig. 2. Position of the strain gauges bonded onto the knife blade.

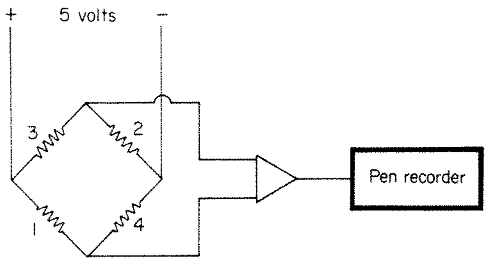


Fig. 3. Schematic wiring diagram of the strain gauges. Pair 1 and 2 is balanced against pair 3 and 4.

grip for the thumb. The flat part of the blade thus forms a stiff spring which is distorted by the thumb during adduction. The transducer is fixed to the hand in the position shown in Fig. 1 with the aid of adhesive tape.

Four strain gauges (Type II, No. 308102, R. S. Components) are bonded as pairs using cyanoacrylate glue on either side of the flat part of the blade (which should, therefore, be at least 13 mm long to accommodate them), as shown in Fig. 2. Figure 3 illustrates the gauges connected as a Wheatstone bridge. This will be in balance provided the surface is flat. The supply and output cables are led along the knife handle. The assembly is covered with cold setting silicone rubber and then enclosed in a heat-shrink sleeving to achieve insulation. When the flat part of the blade is distorted by adduction of the thumb an imbalance results in the Wheatstone bridge which is suitably amplified and recorded on a conventional pen/chart recorder. The bridge supply voltage is 5 volts.

Discussion

Some communications have stressed the need for attention to detail when transducers are positioned and aligned for monitoring neuromuscular blockade.[2-5] The transducer we have described can be attached easily and rapidly and its sensitivity to subsequent changes in posture is not high; even when a patient is turned from

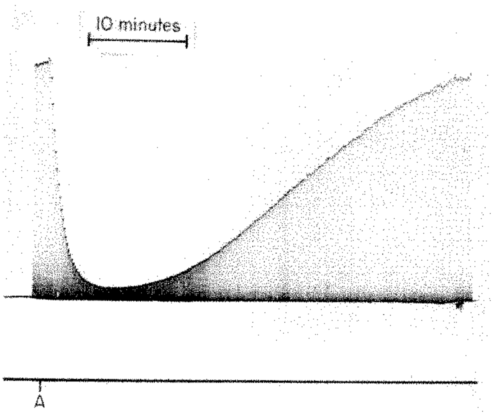


Fig. 4. A typical recording for a single twitch applied at 10-second intervals. Atracurium 0.3 mg/kg was injected at A; the onset of blockade and subsequent spontaneous recovery are shown.

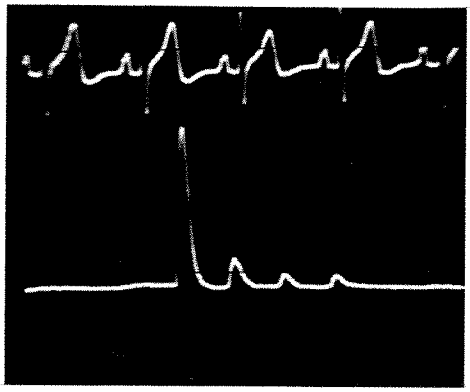


Fig. 5. A monitor screen that displays a fading train-of-four response on the second channel; the first channel is occupied by an ECG trace.

supine to prone there is minimal baseline disturbance. Figure 4 shows a complete recording obtained in response to single twitch 0.1 Hz stimulation following a single dose of atracurium when the paper speed was 1.5 mm/minute. Evoked responses for other stimuli such as tetanus (50 Hz) and train of four (2 Hz) are recorded equally well.

The evoked responses can also be visualised on a conventional ECG screen if the amplified bridge output is fed into the second channel of a cascade monitor (Fig. 5). Freezing the cascade provides an ideal method for the assessment of train-of-four ratios. The screen display also affords a view of the thumb's response to stimulation even when the thumb itself is inaccessible or hidden.

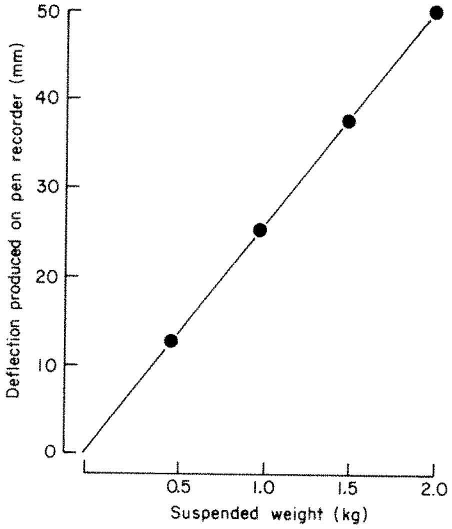


Fig. 6. Repeated calibration of the apparatus has revealed identical deflections on the pen recorder; thus, consistent linearity is confirmed.

During the 2-year period that the device has been in use the recorded output from the transducer has been shown to be consistently linear over the range 0 – 2 kg. To demonstrate this linearity the knife handle is clamped in the vertical position and known weights are suspended, with thread, from the blade tip. The resultant deflections produced on the pen recorder have remained identical throughout the period, as shown in Fig. 6, which illustrates the results of five separate calibrations.

Acknowledgments

We are grateful to Mr J. Halliday of the Department of Biomedical Physics and Bio-Engineering, Aberdeen University for technical assistance and to Mrs A. Gordon for typing the manuscript.

Note

The components are available from:

R. S. Components,
P.O. Box 99,
Corby, Northants.

and comprise:

4 Bonded Strain Gauges Type II: RS 308102 at £2.40 each

Strain Gauge Amplifier: RS 308815 at £25.50
Printed Circuit Board: £2.57
Encapsulated Power Supply (optional): RS 591102 at £40.00

References

1. KATZ RL. Comparison of electrical and mechanical recording of spontaneous and evoked muscle activity. *Anesthesiology* 1965; **26:** 204–11.
2. WALTS LF, LEBOWITZ M, DILLON JB. A means of recording force of thumb adduction. *Anesthesiology* 1968; **29:** 1054–5.
3. ALI MM, SAVARESE JJ. Monitoring of neuromuscular function. *Anesthesiology* 1976; **45:** 216–49.
4. VIBY-MOGENSEN J. Clinical assessment of neuromuscular transmission. *British Journal of Anaesthesia* 1982; **54:** 209–23.
5. TYRELL MF. The measurement of the force of thumb adduction. *Anaesthesia* 1969; **24:** 626–9.
6. ALI MM. A new device for monitoring force of thumb adduction. *British Journal of Anaesthesia* 1970; **42:** 83–5.
7. WALTS LF. The 'Boomerang'—a method of recording adductor pollicis tension. *Canadian Anaesthetists' Society Journal* 1973; **20:** 706–8.
8. BARAKA A. Monitoring of neuromuscular transmission in anesthetised man by a bulb transducer assembly. *Anesthesia and Analgesia* 1973; **52:** 36–8.

Anaesthesia, 1987, Volume 42, pages 1096–1097

HISTORICAL

Sir Ivan Magill

A supplementary bibliography

H. A. CONDON

Summary

Further annotated references to the life and work of Sir Ivan Magill are listed.

Key words

History; Magill.
Intubation; tracheal.

On the occasion of the late Sir Ivan Magill's 90th birthday, Bryn Thomas compiled a bibliography[1] of his work. Thomas did not claim that it was comprehensive but study shows that it is virtually complete. This supplement comprises one reclassified paper and some further references.

1. MAGILL IW. Modern views on anaesthesia. *Newcastle Medical Journal* 1934; **14:** 67–78.

This is No. 59 in Thomas' listing and should really be reclassified into the section on anaesthesia for thoracic surgery. The original bronchial intubation is generally attributed to Gale and Waters[2] in 1931. Archibald,[3] acting on a suggestion of Harold Griffith, is considered to have pioneered the use of bronchial blockers in a paper read in June 1934. However, in this lecture given in Newcastle on 1 February 1934, Magill clearly describes the use of a coudé cuffed bronchial suction catheter in anaesthesia for lobectomy. It is impossible to say to what extent, if at all, Magill and Archibald were in contact.

2. MAGILL IW. Anaesthesia. In: SHEEHAN JE, ed. *Plastic surgery of the orbit.* New York: Macmillan, 1927.

He advocates 'double tube' tracheal insufflation and illustrates an expiratory attachment for catheters for use in children under 2 years where the glottis is not big enough to take an expiratory tube. Sheehan was an American plastic surgeon who worked at Sidcup after World War I and tried to persuade Magill and Rowbotham to emigrate to the USA.[4]

3. MAGILL IW. Foreword to: NOSWORTHY MD. *The theory and practice of anaesthesia.* London: Hutchinson, 1935.

4. JOHNSON B. Anaesthesia in endoscopy. *Journal of Laryngology and Otology* 1939; **54:** 412–28.

This is a report of a meeting of the Section of Laryngology of the Royal Society of Medicine on 3 January 1939. Magill contributed to the

---

H.A. Condon, FFARCS, Consultant (Retired), Department of Anaesthetics, The Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London WC1X 8DA.

0003–2409/87/101096 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

discussion and emphasised the value of the Chevalier Jackson 'Sermon on relaxation'. In his view, local anaesthesia was the safest and should be the first choice.

5. Magill IW. Anaesthesia. In: Millin T, ed. *Retropubic urinary surgery*. Edinburgh: Livingstone, 1947.

Here, Magill advocates intermittent thiopentone (maximum total dose 1 gram) nitrous oxide/oxygen anaesthesia supplemented by cyclopropane or chloroform if necessary. If the blood urea is high, local analgesia was recommended. If an anaesthetist was not available, the surgeon should undertake spinal analgesia.

6. Magill IW. Anaesthesia. In: Gillies H, Millard DR, eds. *The principles and art of plastic surgery*. London: Butterworth, 1957.

This chapter contains pictures of Magill performing blind nasal intubation and emphasises the 'sniffing the morning air' position and the importance of listening to the breath sounds through the tube. It concludes with an account of Gillies operating on a patient with asymmetrical breasts. After prolonged suturing and resuturing, he stood back to await the approval of the visitors. Magill's voice was then heard: 'Surely the same effect could have been achieved with a thick sole on her right shoe'.

7. Magill IW. Tribute to Stanley Rowbotham. *British Medical Journal* 1979; **1:** 1348.

Magill's appreciation, for Stanley Rowbotham's obituary, would appear to be his last writing. However, in the event, at his advanced age, he did not feel equal to the task which was therefore undertaken by a ghost writer.

8. Bowes JB, Zorab JSM. Sir Ivan Magill's contribution to anaesthesia. In: Rupreht J, van Lieburg MJ, Lee JA, Erdmann W, eds. *Anaesthesia—essays on its history*. Berlin: Springer, 1985.

This provides a good general summing-up based on Rowbotham's biographical paper[5] although the author's suggestion that Magill's prowess at blind nasal intubation was partly due to muscular strength is questionable to say the least.

9. *Obituary*

The Times	29 November 1986
Daily Telegraph	29 November 1986
British Medical Journal	1987; **294:** 62–3
The Lancet	1987; **1:** 55
Anaesthesia	1987; **42:** 231–3

Reference should also be made to the technique of regional analgesia for thoracoplasty with which the names of Magill and Semb[6] are associated. Semb was a Norwegian thoracic surgeon who was responsible for the development of extrafascial apicolysis as part of thoracoplasty. Later, he became Professor of Surgery in Oslo. Magill visited him and brought the details of the regional analgesia technique back to England (Dr R. Mansfield, personal communication). He appears not to have published this material.

References

1. Thomas KB. Sir Ivan Whiteside Magill, KCVO, DSc, MB, BCh, BAO, FRCS, FFARCS(Hon), FFARCSI(Hon), DA. A review of his publications and other references to his life and work. *Anaesthesia* 1978; **33:** 628–34.
2. Gale JW, Waters RM. Closed endobronchial anaesthesia in thoracic surgery; preliminary report. *Journal of Thoracic Surgery* 1932; **1:** 432–7.
3. Archibald E. A consideration of the dangers of lobectomy. *Journal of Thoracic Surgery* 1935; **4:** 335–51.
4. Condon HA, Gilchrist E. Stanley Rowbotham. Twentieth century pioneer anaesthetist. *Anaesthesia* 1986; **41:** 46–52.
5. Rowbotham S. Ivan Magill. *British Journal of Anaesthesia* 1951; **23:** 49–55.
6. Lee JA. *Synopsis of anaesthesia*. Bristol: Wright, 1947.

Anaesthesia, 1987, Volume 42, pages 1098–1101

Forum

An epidural infusion technique for labour

D.G. Gaylard, BSc, FFARCS, I.H. Wilson, MB, ChB, FFARCS, Registrars, H.G.R. Balmer, MD, FFARCS, Consultant, Department of Anaesthetics, Freedom Fields Hospital, Plymouth, Devon.

Summary

A regimen to facilitate control of epidural infusions in labour has been developed which allows midwives to alter infusion rates to maintain satisfactory analgesia. The technique was used successfully in 30 patients and, in a prospective study, was compared with women who received conventional top-up epidurals. It was found that infusions provided comparable analgesia and decreased midwife workload but resulted in a higher dosage of bupivacaine.

Key words

Analgesia; obstetric.
Anaesthetic techniques, regional; epidural.

In the UK, epidural analgesia in labour is usually provided by anaesthetists who give the first dose of local anaesthetic via a catheter in the epidural space. Subsequent doses or top-ups are frequently given by midwives. Occasionally, problems may arise during epidural analgesia and considerations of patient safety are paramount.

The continuous epidural infusion of bupivacaine is an established method of providing analgesia[1–4] and has been noted to reduce medical staff workload when compared with a conventional top-up technique.[5] An element of increased safety may also result because the number of bolus injections into the epidural space is reduced. Our hospital delivers around 5500 patients each year and the epidural rate for labour is 19%; top-ups are performed by trained midwives. We elected to try epidural infusions in this setting and devised an infusion technique to meet certain specific requirements for patient safety, efficacy and midwife control of the infusion.

Bupivacaine concentrations from 0.125 to 0.3% are regarded as optimum for infusion by various workers.[1,3,4,6] We chose 0.25% since, in a pilot study, this concentration provided good analgesia but acceptably little motor block.

Methods

A flow chart based on hourly clinical observations was developed in order to facilitate midwife control of the infusion (Fig. 1). The rate of infusion was altered according to a prescription chart (Table 1) and, once in place, was regulated by midwives unless a problem developed, when an anaesthetist was called.

A pilot study was conducted in 15 patients to check the efficacy of the technique. We then compared 30 primigravidae who received conventional epidurals with 30 who received our infusion technique. Only primigravidae whose labour was expected to last a further 4 hours were included. Thirty consecutive patients who met these criteria were given infusions and the following 30 patients were given top-up epidurals.

All patients received 500–1000 ml preload of Hartmann's solution intravenously. The epidural space was identified by loss of resistance to air, using the midline approach and a 16-gauge Tuohy needle. In all cases a Portex epidural catheter was inserted; 2–4 cm were left in the epidural space and an epidural filter (Millex 0.22μ) was connected in series. Each mother then received 8–10 ml (including the 3-ml test dose) of 0.5% plain bupivacaine.

Correspondence should be addressed to Dr H.G.R. Balmer please.

0003–2409/87/101098 + 16 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

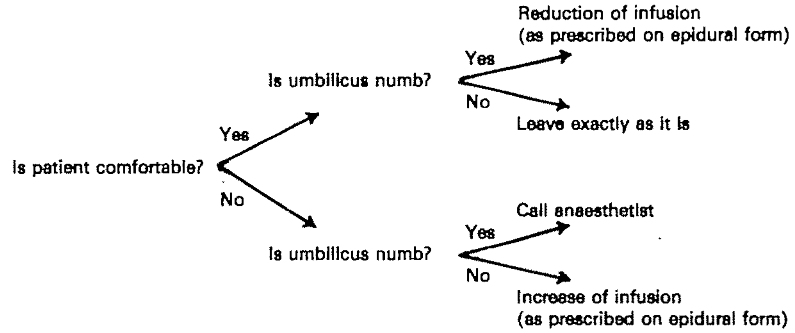


Fig. 1. Flow chart for midwife control of continuous epidural infusion.

Table 1. Infusion prescription details.

Initial infusion rate	*X* ml/hour 0.25% bupivacaine
Increase required	Give bolus of 5 ml 0.5% bupivacaine and increase infusion by 2 ml/hour to a maximum of 9.9 ml/hour
Decrease required	Stop infusion for 15 minutes and reduce infusion rate by 2 ml/hour

Mothers in the top-up group received 10 ml 0.25% plain bupivacaine as required by our standard top-up technique, given by trained midwives. Thirty minutes after the initial dose of bupivacaine, if analgesia was satisfactory, the mothers in the infusion group received an infusion of 0.25% plain bupivacaine at between 7 and 9 ml/hour using a Vickers Treonic syringe driver. Patients below 153 cm height were given the lower first dose and infusion rate. Portex manometer tubing was used to connect the syringe to the filter. The mothers were assessed formally at hourly intervals when the midwives noted the quality of analgesia, arterial blood pressure and sensitivity of the umbilicus to pin prick. The latter was used to detect ascending block and, thus, as one index for altering the infusion rate. The first assessment was carried out one hour following the commencement of the infusion.

Workload. We wished to assess the midwife and medical staff workload in these mothers and, after discussion with the nursing staff and timing of the tasks involved, performance of each task was given a standard time. A standard top-up (which involves checking drugs and administration of local anaesthetic and subsequent observations) was determined to take at least 30 minutes (often longer, since trained staff may not be immediately available). Single blood pressure measurements were estimated to take one minute and umbilicus sensitivity tests, 30 seconds. Medical staff workload involved an extra 15 minutes to set up an infusion.

Bupivacaine dosage. The total dose of bupivacaine and the dose/hour for labour were recorded for each patient in both groups. The additional dose of bupivacaine to provide surgical analgesia for Caesarean section was not included in these totals.

The following data were also collected: duration of the epidural from siting to delivery; quality of analgesia; mode of delivery; infant Apgar scores at 1 and 5 minutes; and duration of motor block, which was regarded as prolonged if the patient was unable to stand 6 hours after delivery.

Mean values and standard deviations were calculated for each group and the results subjected to Student's *t*-test for unpaired data, where appropriate; probability was referred to the two-tailed case.

Results

Sixty primigravid patients were studied. The two groups were comparable in terms of age, height, labour and duration of epidural analgesia but differed in booking weight.

Midwife workload. Midwife workload was reduced in the infusion group (Table 2). The difference was statistically significant ($p < 0.001$). Medical workload was increased.

Bupivacaine dosage. The total dose of bupivacaine was higher in the infusion group than in the top-up group (Table 2). In order to compare the different bupivacaine requirements between the two groups, doses were expressed as mg/kg booking body weight/labour. The dose was significantly higher in the infusion group ($p < 0.001$). Nineteen patients in the infusion group required small (5 ml) top-ups in addition to the infusion. Only two patients in the infusion group required more than one top-up (two each).

Maternal and infant outcome. In the top-up group 28 of the patients regarded their analgesia as good or adequate compared with 29 in the infusion group (Table 3). The modes of delivery were similarly divided between the groups. There were no significant differences in the Apgar scores at 1 and 5 minutes between the two groups. Prolonged motor block occurred in five patients in the top-up group and four patients in the infusion group.

Table 2. Patient data, dose of bupivacaine and midwife workload. Values expressed as mean (SD).

	Top-up patients	Infusion patients	Statistical significance
Number of patients	30	30	
Age, years	23 (4.12)	24.1 (4.6)	NS
Booking weight, kg	59 (8.8)	65.1 (9.2)	$p < 0.02$
Height, cm	160.6 (6.7)	163.3 (6.48)	NS
Duration of epidural, hours	6.2 (3.3)	6.5 (3.3)	NS
Total dose, mg	110.5 (54.2)	197.9 (63.4)	$p < 0.001$
mg/booking weight, kg/labour	1.87 (0.88)	3.09 (1.12)	$p < 0.001$
Midwife workload, minutes/labour	76.5 (61.3)	35.2 (19.7)	$p < 0.001$

NS, Not significant.

Table 3. Maternal and infant outcomes.

		Top-up patients	Infusion patients
Analgesia	Good	22	25
	Adequate	6	4
	Poor	2	1
Mode of delivery	SVD	13	13
	Liftout forceps	7	6
	Keillands	5	4
	Caesarean section	5	7
Apgar scores			
1 minute	Mean	8.4	8.2
	0–2	0	0
	3–6	3	3
	7–10	27	27
5 minutes	Mean	9.0	9.0
	0–2	0	0
	3–6	1	1
	7–10	29	25*
Prolonged motor block		5	4

* Four babies whose 1-minute Apgar score was 9 did not have the 5-minute score recorded. No significant differences between groups.

Discussion

The use of continuous epidural infusions of bupivacaine to provide analgesia in labour appears to have attractive advantages in terms of constant analgesia and greater haemodynamic stability.[2,7] The technique has previously been shown to reduce demands on medical time in maintenance of the epidural.[5] Our experience in a hospital where midwives perform top-ups, however, shows that medical workload is increased. This is due to the extra 15 minutes it took us on average to obtain the equipment and to set up the infusion. Midwife workload is, however, decreased and this is related purely to the number of top-ups avoided.

To avoid the possibility of accidental epidural infusion of oxytocics or intravenous infusion of bupivacaine, we decided not to use standard intravenous infusion sets with Ivac controllers since these were already in use for infusion of syntocinon. We used the Vickers Treonic IP3 infusion pump which we found suitable; its only drawback is the ability to infuse at 99.9 ml/hour. Our Medical Physics Department, with Vickers' approval, fitted IP2 control blocks to the IP3 pumps in order to limit the rate to 9.9 ml/hour.

Dural puncture by the catheter during epidural analgesia has been described[8] and is a point of concern. We would hope to detect an ascending block due to intrathecal infusion by limitation of the infusion rate, simple hourly tests of sensory level and half-hourly checks of blood pressure. Reduction in the number of top-ups helps to minimise the danger of misplaced catheters.

We elected to test for ascending block by checking for intact sensation at the umbilicus, which is supplied by the tenth thoracic nerve. The afferent nerve supply of the uterus usually enters the spinal cord at the level of the eleventh and twelth thoracic dermatomes, so a local anaesthetic block at or just below the umbilicus provides analgesia for the first stage of labour. This method proved entirely satisfactory in practice. The mean durations of labour were 6.2 and 6.5 hours respectively in the two groups, so the 60-ml syringe used for the infusion usually sufficed for the entire period of labour.

Portex manometer tubing was used to connect the syringe to the filter because its rigidity guards against kinking or puncture and it is easily distinguished from other infusions to the patient. No patient objected to being linked to a pump. However, if care is not taken when syringes are changed an air lock may be caused in the filter, which will stop the infusion pump. This occurred on one occasion.

Only trained midwives may administer top-ups and this task places considerable demands on their time. Thus, there may be delay in patients receiving their top-up which results in fluctuating and often inadequate analgesia. It is difficult to judge how much of a problem this was, since no difference was found when the patients were questioned. The reduction in midwife workload has considerable advantages in a busy maternity unit and midwives were generally enthusiastic about the technique.

The higher mean total dose of bupivacaine in the infusion group may be a source of anxiety but is comparable with that found by other workers. Two patients in this group received more than 300 mg and their epidural infusions were maintained for longer than 14 hours. Three patients in the infusion group proceeded to Caesarean section under epidural block and the extra bupivacaine dose required to provide surgical analgesia in this situation led to doses greater than the maximum recommended by theoretical considerations.[9] Our findings agree with those of other workers,[4] that it is the total dose of local anaesthetic in the extradural space, rather than the volume, that is the decisive factor during continuous infusions. Maternal and infant outcome showed no differences between the two groups.

References

1. Evans KRL, Carrie LES. Continuous epidural infusion of bupivacaine in labour: a simple method. *Anaesthesia* 1979; **34:** 310–5.
2. Clark MJ. Continuous mini infusion of 0.125 per cent bupivacaine into the epidural space during labor. *Journal of the American Osteopathic Association* 1982; **81:** 484–91.
3. Taylor HJC. Clinical experience with continuous epidural infusion of bupivacaine at 6 ml per hour in obstetrics. *Canadian Anaesthetists' Society Journal* 1983; **30:** 277–85.
4. Li DF, Rees GAD, Rosen M. Continuous extradural infusion of 0.0625% or 0.125% bupivacaine for pain relief in primigravid labour. *British Journal of Anaesthesia* 1981; **57:** 264–70.
5. Caldwell JE, Braidwood JM. Epidural analgesia by infusion. *Anaesthesia* 1984; **39:** 493–4.
6. Kenepp NB, Cheek TG, Gatsche BB. Bupivacaine: continuous infusion epidural analgesia for labor. *Anesthesiology* 1983; **59:** A407.
7. Abboud TK, Afrasiabi A, Sarkis F, Daftarian F, Nagappala S, Noveihed R, Kuhnert BR, Miller F. Continuous infusion epidural analgesia in parturients receiving bupivacaine, chloroprocaine or lidocaine: maternal, fetal and neonatal effects. *Anesthesia and Analgesia* 1984; **63:** 421.
8. Phillip JH, Brown WU. Total spinal anesthesia late in the course of obstetric bupivacaine epidural block. *Anesthesiology* 1976; **44:** 340–1.
9. Reynolds F, Hargrove RL, Wyman JB. Maternal and foetal plasma concentrations of bupivacaine after epidural block. *British Journal of Anaesthesia* 1973; **45:** 1049.

Anaesthesia, 1987, Volume 42, pages 1101–1104

The Triservice anaesthetic apparatus

Trial of isoflurane and enflurane as alternatives to halothane

M. Kocan, MB, BCh, FFARCS, Senior Specialist in Anaesthesia, 23 Parachute Field Ambulance RAMC, Rhine Barracks, Aldershot, Hants.

Summary

Sixty male patients undergoing limb surgery were anaesthetised using a drawover technique with the Triservice apparatus. They were randomly allocated to receive trichloroethylene and one of three other volatile agents (halothane, enflurane or isoflurane) after thiopentone induction. Signs of inadequate anaesthesia were noted. The incidence of such signs was not significantly different in the three groups. Similarly, no qualitative difference could be demonstrated in the immediate recovery, but the recovery time was significantly shorter with enflurane.

Key words

Equipment; Triservice anaesthetic apparatus.

The apparatus used was first described in 1968.[1] It comprises two Oxford Miniature Vaporizers (OMV) in series to provide halothane for hypnosis and trichloroethylene as the analgesic element of a balanced anaesthetic technique (Fig. 1). Since the adoption of this apparatus by field surgical units of the British

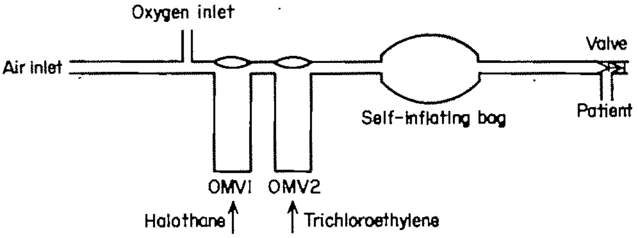


Fig. 1. The Triservice apparatus.

Table 1. Patients' ages, weights and duration of surgery.

	Halothane ($n = 20$)			Enflurane ($n = 20$)			Isoflurane ($n = 20$)		
	Mean	Range	SD	Mean	Range	SD	Mean	Range	SD
Age, years	31	17–46	10.1	30	17–46	9.5	29	17–44	7.6
Weight, kg	72	51–93	11.4	76	47–95	13.4	77	63–99	9.2
Duration, minutes	47	7–90	21	41	16–77	20	51	22–75	19

Table 2. Incidence of signs of inadequate anaesthesia.

	Halothane	Enflurane	Isoflurane
Coughing	2	3	5
Laryngospasm	0	1	3
Movement in response to surgery	1	3	2
Total events	3	7	10
Number of patients	3	5	8

armed forces, it has become known as the Triservice apparatus. The purpose of this study was to assess the suitability of isoflurane and enflurane as the hypnotic components of the system.

Methods

All patients were male, ASA grades 1 and 2, aged between 17 and 46 years. Patients were selected who required limb surgery of anticipated duration less than 90 minutes. Ethical committee approval was obtained. Premedication consisted of papaveretum and perphenazine according to weight, one hour prior to surgery.

The Triservice anaesthetic apparatus was used in all cases. Ambient air was supplemented with an oxygen flow of 1 litre/minute. Six OMVs were used, one for each anaesthetic vapour and three for trichloroethylene. All vaporizers were calibrated and the oxygen concentration was measured downstream of the vaporizers. A Ruben's patient valve was used and its outlet attached to an anaesthetic gas scavenging system.

Anaesthesia was induced with thiopentone 5 mg/kg given over 20–30 seconds. Ventilation was supported during the initial apnoea following induction but was not required for more than 2 minutes. Anaesthetic vapours were introduced during the period of controlled ventilation and continued on the return of spontaneous ventilation.

All patients received 0.5% trichloroethylene for the duration of anaesthesia. In addition, all patients received halothane, isoflurane or enflurane; the concentration was adjusted to provide clinically satisfactory anaesthesia. All anaesthetics were administered by the author.

The incidence of signs of inadequate anaesthesia, coughing, laryngospasm and movement in response to surgery during anaesthesia was recorded. Increments of thiopentone 1.5 mg/kg were administered in response to persistent problems.

In the immediate recovery period the occurrence of coughing, laryngospasm, vomiting and delirium was recorded. The time when patients were able to answer simple questions was noted. The recovery time was taken as the time between discontinuation of the volatile agents and the return of this ability. These observations were performed by recovery room staff who were individually instructed by the author. The volumes of each anaesthetic agent used were also measured.

The distributions of patient age and weight and the duration of anaesthesia were compared using multiple paired t-tests to ensure comparability of the three groups. In addition, the distributions of recovery time and the inspired oxygen concentrations were also compared using multiple t-tests. The Chi-squared test was used to compare the incidence of signs of inadequate anaesthesia and of problems in the immediate recovery period.

Results

The twenty patients in each group were comparable in respect of age, weight and duration of anaesthesia (Table 1). The incidence of signs of inadequate anaesthesia and the number of patients who required incremental doses of thiopentone are shown in Tables 2 and 3. These results did not attain statistical significance. Two patients, one who received enflurane and one given isoflurane, were considered to have persistently inadequate anaesthesia until the administration of fentanyl 50 μg intravenously.

The numbers of patients in each group who showed complications in the immediate recovery period are shown in Table 4. There was no statistical difference between the groups.

No significant difference was found in the recovery

Table 3. Additional thiopentone requirements.

	Halothane	Enflurane	Isoflurane
Number of extra increments	1	6	8
Number of patients	1	5	7

Table 4. Incidence (number of patients) of complications that occurred during the immediate recovery period.

	Halothane	Enflurane	Isoflurane
Persistent cough	1	0	0
Laryngospasm	0	0	0
Vomiting	0	0	1
Delirium	1	3	1
Total events	2	3	2
Number of patients	2	3	2

Table 5. Recovery times (minutes).

	Halothane			Enflurane			Isoflurane		
	Mean	Range	SD	Mean	Range	SD	Mean	Range	SD
Recovery time	21	7–43	8	15	6–29	7	23	8–38	7

Table 6. Recovery times (minutes) in supplemented and non-supplemented anaesthesia

	Halothane			Enflurane			Isoflurane		
	n	Mean	Range	*n*	Mean	Range	*n*	Mean	Range
Supplemented	1	17	—	5	17	8–29	8	24	8–33
Non-supplemented	19	21	7–43	15	14	9–27	12	22	8–30

Table 7. Estimated costs of the techniques using the different agents.

	Halothane	Enflurane	Isoflurane
Total volume used, ml	410	480	630
Mean duration of anaesthesia, minutes	47	41	51
Volume			
ml/patient	20.6	24	31.4
ml/45 minutes general anaesthesia	19.7	26.5	27.7
Cost/45 minutes general anaesthesia	£0.79p	£3.52p	£9.26p

Costs are based on basic NHS prices August 1986.

times between those who received halothane and isoflurane (Table 5) but recovery was significantly faster following enflurane than with the other two agents ($p < 0.05$). Recovery times were not significantly affected by incremental doses of thiopentone (Table 6).

Table 7 shows the volumes of the inhalational agents used and the estimated cost per 45 minutes of anaesthesia. Cost was considerably higher when isoflurane was used.

Discussion

The Triservice apparatus has been in use with field surgical units of the Royal Army Medical Corps (RAMC) for some 10 years and has been used in Belize, the Oman, Northern Ireland and the Falkland Islands.[2,3] Until now it has always been used with halothane as the hypnotic component of a balanced anaesthetic technique and, while its users have generally been satisfied with the current arrangement, there are theoretical considerations that would suggest halothane is not the ideal agent.

Halothane has been shown to be more dysrhythmogenic than enflurane or isoflurane in the presence of endogenous or exogenous catecholamines.[4] This may be significant in the choice of agent for use on the acutely traumatised, in whom a high level of endogenous catecholamines might be expected. Battle casualties often need repeated surgery, typically for an initial debridement and subsequent delayed wound closure. In many such instances it has been found impossible to avoid repeated exposure to halothane,[2] with subsequent risk of liver dysfunction. The use of an alternative agent would reduce this risk.

Enflurane and isoflurane, unlike halothane, have demonstrable analgesic activity[5,6] and might therefore be considered as potentially better agents in drawover anaesthesia. Both have been used as sole agents in this way, without the addition of trichloroethylene.[7,8] Consideration of the physical properties of the volatile anaesthetics suggests that enflurane and isoflurane would be characterised by a more rapid induction and recovery.[9] However, previous evaluation of these aspects has yielded contradictory results.[10–15]

This study set out not to clarify these purely theoretical aspects but to assess the performance of enflurane and isoflurane in the Triservice apparatus from the user's point of view. Are these agents practical alternatives to halothane? The author's impression was that halothane was an easier agent with which to obtain satisfactory results but the statistical analysis did not support this impression. Indeed, the conclusion that enflurane and isoflurane are acceptable alternatives is supported by the fact that satisfactory anaesthesia was eventually obtained in all cases.

It is concluded, therefore, that enflurane and isoflurane are both acceptable alternatives to halothane in the Triservice apparatus. However, in view of the shorter recovery time and the enormous cost differences, it is felt that the use of enflurane is preferable to isoflurane.

References

1. Gabbe D, Ozario HPL. Halothane, trichloroethylene and air. *Anaesthesia* 1968; **23:** 705–6.
2. Jowitt MD, Knight RJ. Anaesthesia during the Falklands campaign. The land battles. *Anaesthesia* 1983; **38:** 776–83.
3. Knight RJ, Houghton IT. Field experience with the Triservice anaesthetic apparatus in Oman and Northern Ireland. *Anaesthesia* 1981; **36:** 1112–7.
4. Johnston RR, Eger EI, Wilson C. A comparative interaction of epinephrine with enflurane, isoflurane, and halothane in man. *Anesthesia and Analgesia* 1976; **55:** 709–12.
5. McCleod DD, Ramayya GP, Tunstall ME. Self administered isoflurane in labour. A comparative study with Entonox. *Anaesthesia* 1985; **40:** 424–6.
6. Abboud TK, Shnider SM, Wright RG, Rolbin SH, Craft JB, Henriksen EH, Johnson J, Jones MJJ, Hughes SC, Levinson G. Enflurane analgesia in obstetrics. *Anesthesia and Analgesia* 1981; **60:** 133–7.
7. Tighe SQM. An ideal agent for drawover anaesthesia? *Anaesthesia* 1986; **41:** 1160–1.
8. Hall RM, Boulton TB. Editorial. *Anaesthesia* 1979; **34:** 755–6.
9. Corrall IM. Isoflurane: the need for new volatile agents. Editorial. *Anaesthesia* 1983; **38:** 1035–6.
10. Pandit UA, Steude GM, Leach AB. Induction and recovery characteristics of isoflurane and halothane anaesthesia for short outpatient operations in children. *Anaesthesia* 1985; **40:** 1226–30.
11. Nunn JF. Isoflurane as a routine anaesthetic in general surgical practice. *British Journal of Anaesthesia* 1985; **57:** 461–75.
12. Black GW, Johnston HML, Scott MG. Clinical impressions of enflurane. *British Journal of Anaesthesia* 1977; **49:** 875–80.
13. Carter JA, Dye AM, Cooper GM. Recovery from day case anaesthesia. *Anaesthesia* 1985; **40:** 545–8.
14. Strunin L, Strunin J, Phipps J, Corrall IM. Halothane and enflurane for out patient dental anaesthesia. *British Dental Journal* 1979; **147:** 299–351.
15. Jellicoe JA. A comparison of alfentanil, halothane and enflurane for day case gynaecological surgery. *Anaesthesia* 1985; **40:** 810–2.

Anaesthesia, 1987, Volume 42, pages 1104–1107

Interview method affects incidence of postoperative sore throat

C.J. Harding, MB, ChB, FFARCS, Registrar, F.K. McVey, MB, ChB, Senior House Officer, Department of Anaesthesia, Hereford County Hospital, Hereford HR1 2ER.

Summary

Two hundred and forty-two routine surgical patients who had undergone general anaesthesia, were questioned about postoperative sore throat by one of two methods, either direct or indirect questioning. A significantly higher incidence of sore throat was obtained by direct questioning ($p < 0.001$).

Key words

Complications; sore throat.

Sore throat is a common minor complaint following anaesthesia with or without tracheal intubation. The reported incidence varies widely. There does not seem to be any accepted standard method of eliciting postoperative complaints yet it is highly likely that the method chosen has an important effect on the final

---

Correspondence should be addressed to Dr F.K. McVey, Senior House Officer, Department of Anaesthesia, Southmead Hospital, Bristol BS10 5NB.

Introduction

'Hello, I'm Dr. . . . . ., an anaesthetist. We're doing a survey of some of the after effects of general anaesthetic. Would you mind answering a few questions?
How are you feeling?'

Then either

Direct questioning

'Have you had a sore throat at all since your operation?'
If so, 'Would you call it mild, moderate or severe?'
'Have you any aches, pains or discomfort elsewhere?'
If so, 'Whereabouts is the pain?'

or

Indirect questioning

'Have you had any aches, pain or discomfort at all since your operation?'
If so, 'Whereabouts is it?'
If sore throat, 'Would you call it mild, moderate or severe?
Do you have any other pain or discomfort? Whereabouts?'

This question was repeated and symptoms discussed until all complaints had been elicited.

Finally

4. 'Do you smoke at all?'
If so, 'Approximately how many a day?'

Fig. 1. Interview format used to question each patient.

results. We decided to investigate the difference between asking patients directly and indirectly about postoperative sore throat.

Method

Two hundred and forty-two patients were studied over 4 consecutive weeks. All patients scheduled to undergo elective gynaecological, orthopaedic and general surgery were eligible except those under 15 years old, those who were to undergo day case surgery or surgery that involved the head and neck, or those who received regional or local anaesthesia only. All anaesthetists in the department were involved in the study and agreed not to alter their usual anaesthetic technique, which was recorded on a form at the end of surgery. Questions were limited to include factors suggested by previous workers[1–20] to contribute to the aetiology of postoperative sore throat. The forms were collected at the end of each day but not examined until the postoperative interview had taken place. Each patient was interviewed between 6 and 24 hours after arrival in the recovery room by one of two interviewers. A standardised interview format and wording was used (Fig. 1). The interviewers were of similar appearance (both wore white coats), similar in manner and of the same sex. Each interview was conducted as privately as possible within the ward setting.

The interview format consisted of a general introduction and explanation followed by a general inquiry about the patient's health. After a degree of rapport was thus established, the patient was asked either directly or indirectly, whether he or she had suffered a sore throat at any time since the operation. The patient was also asked about his/her smoking habits. Indirect questioning was continued until it was felt that all postoperative symptoms had been elicited. The patient's response was recorded immediately on a form designed for that purpose. Neither interviewer saw patients whom she had anaesthetised. Ward staff were asked not to prepare the patients inadvertently for the interview.

Table 1. General characteristics of patients and nature of operations.

	Direct group (n = 113)	Indirect group (n = 129)
Male (number)	46	53
Female (number)	67	76
Mean (SD) age, years	53 (20)	50 (19)
Smokers (more than 5 cigarettes daily)	30	40
Operations		
General surgical	48	52
Gynaecological	38	50
Orthopaedic	27	27

Each interviewer worked on alternate days. Interviewer A used the direct technique for 2 weeks, then changed to indirect for the remaining 2 weeks. Interviewer B began with the indirect technique for 2 weeks, then changed to direct for the remaining 2 weeks. Thus, in any week, both interview methods were in use. Results were analysed using the Chi-squared test.

Results

One hundred and thirteen patients were interviewed directly and 129 patients indirectly, a total of 242 patients in the study. No patient refused to be interviewed. The two groups were broadly matched for age, sex and type of operation (Table 1). The majority of operations (75%) lasted less than one hour.

Overall, 28 out of 113 patients complained of sore throat on direct questioning, compared with two out of 129 patients on indirect questioning. This was a highly significant difference (χ^2 = 29.96, $p < 0.001$; 95% confidence interval 22.4–24.0%). Each interviewer's results considered individually, achieved the same degree of significance (χ^2 = 18.72 and 11.62, respectively). Thirty-five out of 113 patients complained spontaneously of dry throat in the direct group, compared with 10 out of 129 patients in the indirect group. This difference was also highly significant (χ^2 = 21.50, $p < 0.001$; 95% confidence interval 13.6–32.8%).

Within the direct group, patients whose tracheas had been intubated were more likely to complain of sore throat (χ^2 = 9.50, $p < 0.001$). Other than this, comparison of the two groups (those who did or did not

Table 2. Matching of direct and indirect groups with respect to factors thought to influence development of sore throat postoperatively.

	Direct group ($n = 113$)	Indirect group ($n = 129$)
Anticholinergic premedication	104	123
Coughed during anaesthetic (not intubated)	6	14
Oropharyngeal airway used	99	109
Nasogastric tube used	9	9
Details of intubation technique		
Relaxant		
suxamethonium	23	34
non-depolarising	50	48
both	9	18
Intubated	65	64
Type of tube		
rubber	60	62
Portex	5	2
Lubricant		
none	—	1
KY jelly	13	14
lignocaine gel	52	49
Spray		
none	51	45
4% lignocaine	10	15
10% lignocaine	4	4
Introducer		
none	62	57
wire stylet	2	6
gum elastic bougie	1	1
Cuff inflated	65	64
Trauma during intubation	7	8
More than one attempt to intubate	6	9
Coughed or bucked on tube	11	19
Head moved while intubated, e.g. change to prone or lateral position	13	13
Pharyngeal suction	50	53

complain of sore throat) did not suggest any other important differentiating factors. In particular, there was no difference between males and females in the postoperative complaint of sore throat.

Factors thought to affect the incidence of postoperative sore throat, for example, anaesthetic technique and amount of trauma, were recorded preoperatively for each patient. The two groups matched closely on all of these (Table 2). In particular, a similar proportion of each group (58% of the direct group and 50% of the indirect group) was intubated. Fifty-three percent of the direct group and 75% of the indirect group were interviewed in the first 12 hours postoperatively ($\chi^2 = 14.40$, $p < 0.001$). The remaining interviews were completed in the first 24 hours postoperatively.

Discussion

Our data show that interview method has a major effect on the recorded incidence of postoperative sore throat. This is reported in the literature to vary from 6–100% in patients whose tracheas are intubated (Table 3) and from 0–22% in nonintubated patients[3,4,13,15,16] following general anaesthesia. We found an incidence of 35% sore throat in intubated patients and 10% sore throat in nonintubated patients (on direct inquiry).

Table 3. Differing incidence in the literature of postoperative sore throat in intubated patients.

Investigators	Sore throat incidence (%)
Hartsell and Stephen, 1964 (1)	5.7
Wolfson, 1958 (2)	18
Edmonds-Seal and Eve, 1962 (3)	36
Conway *et al.*, 1960 (4)	38
Winkel and Knudsen, 1963 (5)	39
Gard and Cruikshank, 1961 (6)	44
Cronin *et al.*, 1973 (7)	60
Wylie, 1950 (8)	70
Baron and Kohlmoos, 1951 (9)	100

This confirms the findings of other studies.[1,3,4,10,11,13–17] The use of suxamethonium also plays a part.[18] Evidence is conflicting about the effects of the lubricant,[1,4,5,6,16,19] topical analgesic spray[1,4] and nasogastric tube.[1,4,6] Suction, anticholinergic premedication, extended head position or movement of the head during operation have also been implicated. An increased incidence of sore throat has been observed in women[1,2] but neither Conway and his colleagues[4] nor our own study support this. Other workers[13–16,20] have examined cuff design. The area of cuff contact with trachael mucosa seems to be more important than the pressure within the cuff in increasing the likelihood of postoperative sore throat. We used red-rubber tubes with low-volume, high-pressure cuffs in most patients. Little information is available on the peak severity and duration of postoperative sore throat. It is generally considered to be a minor complication of the first postoperative 24 hours[21] although Winkel and Knudsen[5] showed that it may last beyond this period. All our interviews were completed within the first 24 hours but significantly more of the indirect group were interviewed early, i.e. between 6 and 12 hours postoperatively.

Interview technique, as a source of variation in incidence of sore throat, has not been investigated although several studies[6,11,22,23] demonstrated a marked difference in the incidence of complaints that are spontaneously volunteered, and those that are elicited subsequently by direct questioning. It is notable that in the literature examined, interview technique is often poorly described and unstandardised. Techniques vary greatly. Some use direct questioning with more or less specified wording.[2,13–17,20] Others use direct questioning[9,19,22] but the wording or protocol is not made specific. Many workers[3–6,11,23] have used indirect questioning with some follow-up of symptoms volunteered by the patient. Edmonds-Seal and Eve[3] used direct question if symptoms were not forthcoming. Fahy *et al.*[24] and Cronin *et al.*[7] used questionnaires, Kaye[25] looked back through the case notes and Wylie's methods[8] are unspecified.

Psychologists have studied the interview process in depth. Richardson[26] comments: 'the interview is notorious for its lack of reliability and its very poor validity . . . the opportunities for error are enormous.' Error may arise in the way questions are formulated, in the personal characteristics of the interviewer, in the overall structure of the interview and in the method used to record the response of the person interviewed. Structured interviews and closed questions (where the answer is limited to a few possibilities by the nature of the question) are considered to give more reliable and more valid information. Open questions, for example, 'How do you feel?', allow a greater range of response from the patient and greater freedom from the bias and expectations of the interviewer. They may help to establish rapport with patients because they are allowed to respond as individuals, and they can provide useful information in more complex situations. Responses to open questions, however, are difficult to record systematically and a certain degree of skill is usually required of the interviewer. Our data illustrate the very large difference in response that results. A 'trailer' effect was recorded incidentally, which further illustrates the importance of the exact wording of the questions used. There was a highly significant increase in complaint of dry throat in the group questioned directly. This was presumably prompted by the word 'throat' in the question put to the patient. They often responded: 'No, it's not sore, but it's very dry.'

Conclusion

The incidence of sore throat after anaesthetic varies greatly according to the interview technique used. Using a standardised technique it was found to be higher in intubated patients than in non-intubated patients. No sex difference was found.

Acknowledgments

We would like to thank Dr G.R. Cooper for her generous and painstaking supervision. This study would not have been possible without the full cooperation we received from all our anaesthetic colleagues at Hereford. Z. Cockram typed our manuscript.

References

1. Hartsell CJ, Stephen CR. Incidence of sore throat following endotracheal intubation. *Canadian Anaesthetists' Society Journal* 1964; **3**: 307–17.
2. Wolfson B. Minor laryngeal sequelae of endotracheal intubation. *British Journal of Anaesthesia* 1958; **30**: 326–32.
3. Edmonds-Seal J, Eve NH. Minor sequelae of anaesthesia: a pilot study. *British Journal of Anaesthesia* 1962; **34**: 44–8.
4. Conway CM, Miller JS, Sudgen FLH. Sore throat after anaesthesia. *British Journal of Anaesthesia* 1960; **32**: 219–23.
5. Winkel E, Knudsen J. Postintubation sore throat. *Anesthesia and Analgesia* 1963; **50**: 92–4.
6. Gard MA, Cruikshank LFG. Factors influencing the incidence of sore throat following endotracheal intubation. *Canadian Medical Association Journal* 1961; **84**: 662–5.
7. Cronin M, Redfern PA, Utting JE. Psychometry and postoperative complaints in surgical patients. *British Journal of Anaesthesia* 1973; **45**: 879–86.
8. Wylie WD. Hazards of intubation. *Anaesthesia* 1950; **5**: 143–8.
9. Baron SH, Kohlmoos HW. Laryngeal sequelae of endotracheal anaesthesia. *Annals of Otolaryngology, Rhinology and Laryngology* 1951; **60**: 767–92.
10. Jensen PJ, Hommelgaard P, Sondergaard P, Eriksen S. Sore throat after operation: influence of tracheal intubation, intracuff pressure and type of cuff. *British Journal of Anaesthesia* 1982; **54**: 453–7.
11. Jones GOM, Hale DE, Wasmuth CE, Homi J, Smith ER, Viljoen J. A survey of acute complications associated with endotracheal intubation. *Cleveland Clinic Quarterly* 1968; **35**: 23–31.
12. Kurer FL, Welch DB. Gynaecological laparoscopy: clinical experience of two anaesthetic techniques. *British Journal of Anaesthesia* 1984; **56**: 1207–12.
13. Loeser EA, Orr DL, Bennett GM, Stanley TH. Endotracheal tube cuff design and postoperative sore throat. *Anesthesiology* 1976; **45**: 684–7.
14. Loeser EA, Machin R, Colley J, Orr DL, Bennett GM, Stanley TH. Postoperative sore throat—importance of endotracheal tube conformity versus cuff design. *Anesthesiology* 1978; **49**: 430–2.
15. Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. *Anesthesiology* 1980; **52**: 257–9.
16. Loeser EA, Stanley TL, Jordan W, Machin R. Postoperative sore throat: influence of tracheal tube lubrication versus cuff design. *Canadian Anaesthetists' Society Journal* 1980; **27**: 156–8.
17. Stock C, Downs JB. Lubrication of tracheal tubes to prevent sore throat from intubation. *Anesthesiology* 1982; **57**: 418–20.
18. Capan LM, Bruce DL, Patel KP, Turndorf H. Succinylcholine-induced postoperative sore throat. *Anesthesia and Analgesia* 1983; **62**: 253.
19. Lund LO, Daos FG. Effects on postoperative sore throat of two analgesic agents and lubricants used with endotracheal tubes. *Anesthesiology* 1965; **26**: 681–3.
20. Stenquist O, Nilsson K. Postoperative sore throat related to tracheal tube cuff design. *Canadian Anaesthetists' Society Journal* 1982; **29**: 384–6.
21. Latto IP, Rosen M, eds. *Difficulties in tracheal intubation.* Baillière Tindall, 1985: 66–74.
22. Alexopoulos C, Lindholm C-E. Airway complaints and laryngeal pathology after intubation with an anatomically shaped endotracheal tube. *Acta Anaesthesiologica Scandinavica* 1983; **27**: 339–44.
23. Hamelberg W, Welch CM, Siddall J, Jacoby J. Complications of endotracheal intubation. *Journal of the American Medical Association* 1958; **168**: 1959–62.
24. Fahy A, Watson BG, Marshall M. Postanaesthetic follow-up by questionnaire: a research tool. *British Journal of Anaesthesia* 1969; **41**: 439–41.
25. Kaye G. Sequelae of anaesthesia. *British Journal of Anaesthesia* 1936; **13**: 157–76.
26. Richardson JA, Dohrenwend BS, Klein D. *Interviewing: its forms and functions.* New York, London: Bassie Books, Inc., 1965.

Anaesthesia, 1987, Volume 42, pages 1108–1110

Antiemetic studies with traditional Chinese acupuncture

A comparison of manual needling with electrical stimulation and commonly used antiemetics

R.G. Ghaly, MB, FFARCS, Research Fellow, K.T.J. Fitzpatrick, MB, FFARCS, Lecturer, J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, Department of Anaesthetics, The Queen's University of Belfast and Department of Clinical Anaesthetics, Belfast City Hospital.

Summary

The application of low frequency (10 Hz) electrical current for 5 minutes to an acupuncture needle placed at the P6 (Neiguan) point is as effective as manual needling in the reduction of emetic sequelae in women premedicated with nalbuphine 10 mg for a minor gynaecological operation carried out under a standard anaesthetic. Both were slightly, but not significantly, better than the antiemetic properties of cyclizine 50 mg.

Key words

Anaesthetic techniques; acupuncture.
Complications; nausea, vomiting.

Workers from this Department have recently demonstrated the ability of traditional Chinese acupuncture, needling at the P6 point, to reduce emetic sequelae in women premedicated with an opioid, undergoing minor operations under a standard anaesthetic.[1–3] Concurrently, we have studed the efficacy of electrical acupuncture and of two commonly used antiemetics, cyclizine 50 mg and droperidol 2.5 mg, and here present our findings.

Method

This was similar to that in previously reported studies,[1,2] except that only one opioid, nalbuphine 10 mg, was used as premedication, given intramuscularly 90 minutes before induction of anaesthesia. In two groups this was given with cyclizine 50 mg or droperidol 2.5 mg. Acupuncture at P6 (Neiguan point) was applied in four groups immediately following premedication. In one group, manual needling was carried out for 5 minutes while in the others, an electric current was applied to the needle from a DC pulsator (Schackman JS 863-4) at either 1000 Hz for 5 minutes or 10 Hz for 5 or 15 minutes. A square waveform was used with a pulse width of 0.25 ms and the output voltage increased until the patient felt a definite, but not uncomfortable, pulsation. The adjuvant treatments were given in random order and one additional group received the premedication only. It was intended to have 31 observations in each group.

Patients were fit women, aged 16–60 years, weight 40–80 kg and scheduled for minor gynaecological operations (lasting 7–12 minutes). All gave verbal consent to the study; they were told that it concerned the efficacy and toxicity of the premedication, with no mention of sickness, but the true nature was revealed at the last postoperative visit. Anaesthesia was with methohexitone and nitrous oxide in oxygen. Patients were visited at the first and sixth postoperative hours (by a worker unaware of the premedicant regimens) and the occurrence of nausea alone, or of vomiting with or without nausea, was noted.

Differences between series were tested by the Chi-squared and Mann–Whitney *U* tests, with the figures for nausea and vomiting combined.

Results

The key was broken after 38 administrations because of a high incidence of sickness following electrical ACP. This showed that five out of the 12 patients who had 1000 Hz stimulation and eight out of the 14 who had 10 Hz for 15 minutes had either nausea or vomiting, compared with only one out of 12 when 10 Hz was applied for 5 minutes. The study was continued with the latter only. Three patients were very distressed after orthodox antiemetics; the key was again broken and showed that these had all received droperidol. The use of this drug was discontinued after 12 administrations (four patients in this series were nauseated postoperatively).

The results in the completed series are given in Table

Table 1. Number of patients who experienced postoperative emetic effects following premedication with nalbuphine 10 mg with or without acupuncture (5 minutes) or cyclizine 50 mg.

	0–1 hours postoperatively			1–6 hours postoperatively		
Adjuvant therapy	Vomiting	Nausea	Nil	Vomiting	Nausea	Nil
Nil	3	14	14	5	12	14
Manual ACP	4	3	24	0	3	28
Electrical (10 Hz) ACP	1	1	29	3	2	26
Cyclizine 50 mg	5	2	24	5	4	22

Vomiting includes instances with or without nausea.

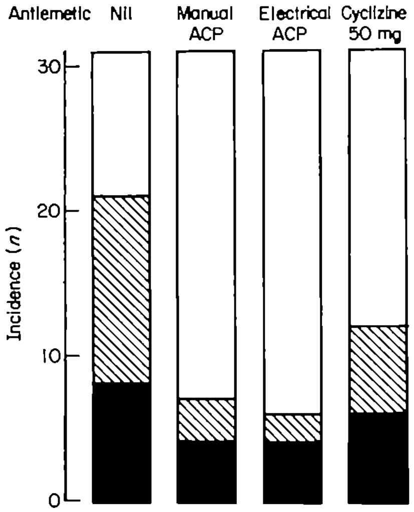


Fig. 1. Total peri-operative vomiting with or without nausea (■) or nausea alone (■) in four groups ($n = 31$) of women undergoing minor operations. Each was pretreated with nalbuphine 10 mg with adjuvant therapy as shown (ACP, acupuncture).

1. No data are given on pre-operative sickness as the incidence is low with nalbuphine. Compared with those given premedication alone, all three forms of treatment reduced the incidence of sickness to a highly significant degree, at all times of observation ($p <$ 0.01–0.0001). Slightly less sickness followed electrical ACP than manual ACP or cyclizine in the first postoperative hour but the differences were not significant and had disappeared by the sixth postoperative hour. Cyclizine appeared to be shorter acting in its antiemetic effect than either ACP technique but, again, the differences were negligible.

Figure 1 gives the incidence of total peri-operative sickness (90 minutes pre-operatively to 6 hours postoperatively) in the four series. Both manual and electrical (10 Hz) ACP caused a highly significant reduction in sickness ($p < 0.0005$), as did cyclizine 50 mg ($p < 0.025$), but there were no significant differences in the incidence of sickness with any of the three forms of therapy.

Excluding the reactions to droperidol, no other side effects were noted in the study. Both acupuncture techniques were well accepted by the patients and, by the end of the study, were accepted as routine practice in the ward unit. Neither technique affected the course of anaesthesia or the dose of methohexitone required.

Discussion

Increasing the number of observations has not altered our previous conclusion that traditional Chinese acupuncture is an effective antiemetic, under the conditions of this study. Electrical stimulation at 10 Hz is equally effective and neither technique differs greatly in its efficacy from that of cyclizine 50 mg. It was impossible to find proven data on the optimal frequency of electrical stimulation for this study. We decided to use the two extremes provided by our apparatus and, clearly, the high frequency had no antiemetic action. When used for other purposes it may induce sickness.[4]

The side effects with droperidol were surprising. It is well known to cause restlessness when given alone[5] but this does not usually occur when combined with an opioid. The situation may be different when a mixed agonist–antagonist drug, such as nalbuphine, is used and this may be worthy of further investigation.

On the basis of this study, low frequency electrical ACP offers an acceptable and possibly more practical alternative to manual needling as an antiemetic. Our combined experience with three opioids and two techniques totalling 110 administrations in a controlled situation, leaves no doubt that P6 ACP is an effective, nontoxic antiemetic under the conditions of this study.

Acknowledgments

We thank our gynaecological and anaesthetic colleagues in the South Belfast Hospitals for their continuing cooperation in these studies.

References

1. Dundee JW, Chestnutt WN, Ghaly RG, Lynas AGA. Traditional Chinese acupuncture: a potentially useful antiemetic? *British Medical Journal* 1986; **293**: 583–4.
2. Dundee JW, Chestnutt WN, Ghaly RG, Lynas AGA. Reduction in emetic effects of opioid preanaesthetic medication by acupuncture. *British Journal of Clinical Pharmacology* 1986; **22**: 214P–5P.

3. Lynas AGA, Ghaly RG, Dundee JW. Acupuncture reduced the emetic effects of nalbuphine premedication. *British Journal of Anaesthesia* 1986; **58:** 1331P–2P.
4. *Manufacturer's Brochure.*
5. Morrison JD, Clarke RSJ, Dundee JW. Studies of drugs given before anaesthesia. XXI. Droperidol. *British Journal of Anaesthesia* 1970; **42:** 730–5.

Anaesthesia, 1987, Volume 42, pages 1110–1113

Unintentional dural puncture. A survey of recognition and management

R.W. Okell, MB, ChB, FFARCS, Registrar, J.S. Sprigge, MB, BChir, FFARCS, Consultant, Arrowe Park Hospital, Upton, Wirral, Merseyside L49 5PE.

Summary

A survey of the recognition and management of 21 unintentional dural punctures that occurred in a series of 3500 obstetric epidurals is presented. In seven cases, dural puncture was not recognised at the time of occurrence and two patients may have subsequently received mixed epidural and subarachnoid analgesia. In two patients with dural puncture in whom air had been used to locate the epidural space, cerebrospinal fluid did not drip from the hub of the needle. A test dose did not reveal incorrect catheter placement in seven patients. The provision of an epidural infusion of Hartmann's solution for 24 hours, together with bed rest, appeared to delay the onset of dural puncture headache rather than prevent it entirely. Blood patching was required only in five of the 21 patients but was entirely successful. The implications of these observations in relationship to obstetric epidural practice are discussed.

Key words

Anaesthetic techniques, regional; epidural.
Complications.

One of the most common major complications of obstetric epidural analgesia is unintentional dural puncture. The incidence should not exceed 2% but it is unlikely to be less than 1% in units in which anaesthetists in training perform epidurals.[1] If recognised immediately, the only important consequence is the frequent occurrence of postspinal headache after delivery. Many measures have been advocated in the prophylaxis and treatment of postspinal headache but only two, the provision of epidural infusions and the use of epidural blood patching, have been shown to be widely beneficial.[2–5]

If dural puncture is not recognised immediately, either by the aspiration of cerebrospinal fluid (CSF) or a profound response to a small test dose of local anaesthetic, there is a risk that the patient will be given a full epidural dose into the subarachnoid space and hence develop a high subarachnoid block. Only prompt resuscitation will avoid fatality in this situation. We here review experience in the recognition and management of dural taps that occurred in an obstetric unit over a period of 4 years.

Methods

Information was collected on all patients whose epidural was complicated by dural tap during a 4-year period. The patients were reviewed on a daily basis and records of symptoms were kept. The majority of patients in whom dural puncture was recognised immediately received an epidural infusion for 24 hours. Blood patching was reserved for patients with persistent headache at 5 days onwards.

Results

Twenty-one dural taps were diagnosed during a period in which approximately 3500 epidurals were performed, an overall incidence of 0.6%. Registrars were responsible for 18 dural taps and consultants for three but the registrars performed 95% of all epidurals. Tough ligaments were regarded as contributory to dural puncture in two cases while excessively soft ligaments, which resulted in difficulty in detecting loss of resistance, were contributory in a further two cases.

Correspondence should be addressed to J.S. Sprigge please.

There was no obvious contributory factor in the remaining 17 cases.

Dural tap was recognised in nine cases because CSF dripped from the needle and in three cases because CSF was aspirated via the epidural catheter. Hypotension occurred after a 2-ml test dose of 0.375% isobaric bupivacaine in two patients.

Headache typical of that following dural tap occurred after delivery in seven patients although there were no discernible signs of mishap at the time of performance or following a test dose. The labour records of these seven patients were reviewed in detail. In one patient, the second top-up (6 ml 0.375% bupivacaine) was followed by marked hypotension (minimum arterial blood pressure 60/20 mmHg) and provided analgesia that lasted more than 3 hours. Hypotension was corrected promptly by fluid administration and 3 mg intravenous ephedrine. In another patient, top-ups of the same volume and concentration were required infrequently (3–4 hours apart) and each produced a small, but clinically insignificant, decrease in blood pressure. A note in the labour record states 'Epidural very effective, no sensation at all'. It seems possible that these two patients received mixed epidural and subarachnoid blocks. One patient had a brief period of hypotension following her third top-up but aortocaval compression may have contributed to this. The remaining four patients illustrated no features in the course of their epidurals to suggest that the dura was breached. Nevertheless, the symptoms displayed postdelivery by these patients were sufficiently characteristic of dural puncture to convince us of the diagnosis. Indeed, two of them subsequently benefitted from blood patching.

All but two of the epidurals complicated by dural puncture were performed using a loss of resistance to injection of saline technique. The remaining two epidurals were performed using loss of resistance to air. In neither of these cases did CSF appear through the needle. One case was detected by hypotension following a test dose and the other, by the development of typical postspinal headache.

Eight patients were delivered electively by forceps as a prophylaxis against postspinal headache and a further three patients were delivered by forceps for unrelated reasons, making 11 forceps deliveries in all. Four patients were delivered by Caesarean section and one patient had an assisted breech delivery; the five remaining patients delivered normally. All but one patient received epidural analgesia following dural puncture and, of these 20 patients, 17 regarded the epidural to have provided good analgesia during labour.

Eleven patients received an epidural infusion of 1000 ml Hartmann's solution over 24 hours as prophylaxis against headache. They were nursed flat initially and then allowed to mobilise gradually. Oral paracetamol was available to them as required. This group included eight patients who were delivered by forceps, two patients who were delivered by Caesarean section and one patient who underwent assisted breech delivery.

Ten patients did not receive an epidural infusion as part of their management. This group included all seven patients whose dural tap was diagnosed retrospectively. In these patients bed rest was instituted at the onset of headache, whereas bed rest was used prophylactically when dural puncture had already been diagnosed. Bed rest was continued for 24 hours followed by graded mobilisation. Oral paracetamol was provided as necessary. Five patients in this group delivered normally, three had forceps and two underwent Caesarean section.

Table 1. Frequency of headache following dural puncture in patients with and without epidural infusion of Hartmann's solution (see text for other differences in management).

Days postdelivery	With epidural infusion ($n = 11$)	Without epidural infusion ($n = 10$)
0	0	2
1	2	8
2	4	8
3	5	9
4	6	7

Table 1 illustrates the frequency of headache in the two groups of patients in the first 4 days following delivery. The incidence of spinal headache at one day postdelivery differed significantly between patients who received an epidural infusion and those who did not (Fisher's exact test, $p = 0.015$), although this difference was absent 4 days postdelivery. However, the management of the two groups of patients differed in other respects, as indicated above.

Table 2. Frequency of headache following dural puncture according to mode of delivery.

Days postdelivery	Operative delivery ($n = 14$)	Normal delivery/breech ($n = 7$)
0	0	2
1	5	5
2	7	5
3	7	7
4	7	6

Table 2 illustrates the frequency of headache in the first 4 days after delivery for the patients grouped according to mode of delivery. Assisted breech delivery is grouped with normal delivery since it is associated with bearing down in the second stage, unlike forceps delivery and Caesarean section. All the patients after normal or breech delivery suffered headache at some stage in the puerperium, as opposed to only seven out of 14 patients who suffered headache after forceps or Caesarean section. However, a much larger proportion of patients in the latter group received epidural infusion as prophylaxis. Patient numbers are too small to justify further breakdown.

Neckache occurred in association with headache in seven out of the 21 patients. Photophobia occurred in only three patients and was never marked. Blood patching was offered to patients with continuing severe headache at 5 days onwards and was undertaken in three patients who had received an epidural infusion and in two patients who had not. The measure was rapidly effective in all cases. Dural tap appears to have been the sole reason for extended hospital stay (greater than 6 days) in 12 of the 21 patients.

Discussion

The frequency of dural puncture in this series compares favourably with that reported in previously published work.[5,6] However, dural tap was not always recognised at the time of occurrence and seven of the 21 cases were diagnosed retrospectively. This finding emphasises the need for constant vigilance if high subarachnoid blocks are to be avoided.

Cerebrospinal fluid dripping from the needle or catheter is normally a clear indication of dural puncture but confusion may arise if loss of resistance to saline is used. The emerging fluid can be tested for temperature, pH and glucose content with the intention of distinguishing CSF from saline but no test is entirely reliable. A loss of resistance to air technique might be expected to make the diagnosis more clear-cut. However, in two patients in whom the method was used, CSF was not seen to emerge from the needle or the catheter.

There has been some controversy about the choice and quantity of local anaesthetic used as a test dose to detect subarachnoid placement of the epidural catheter.[7–12] In this series, the test dose used was 2 ml 0.375% isobaric bupivacaine. This test dose aided the diagnosis in two patients but did not produce a response in seven other patients subsequently diagnosed as having suffered dural tap.

There is some evidence in two patients to suggest that a mixed epidural and subarachnoid block was provided. Similar cases have been recorded.[13,14] It has been noted previously that when a catheter with multiple side holes is in use, some holes may lie in the epidural space and some within the subarachnoid space. Variable response may occur depending on the force applied during injection through the catheter.[15] The routine use of sensory and motor tests after each top-up would aid recognition of this complication. Some authors recommend that every top-up should be preceded by a test dose or given in fractions.[16,17]

The four patients who developed typical dural puncture headache postdelivery but who had no signs of dural puncture during labour are of interest. One explanation for the phenomenon could be that the dura was nicked by the tip of the needle and yet the catheter was still threaded outside the dura. Alternatively, the tip of the catheter may have breached the dura while the side holes remained extradural. The occurrence of unexpected headache should provide an additional reason to review all recipients of epidurals on the day following delivery.

Some of the patients in this series were subjected to elective forceps delivery on the basis that reduced bearing down in the second stage of labour might lessen the incidence of spinal headache. The validity of this practice has been questioned.[1,18] Patients who underwent forceps or Caesarean section had a reduced incidence of headache compared to those who delivered normally or by assisted breech, but differences in management between the two groups make the data difficult to evaluate.

The data presented suggest that the combination of epidural infusion, initial bed rest and elective forceps delivery tends to delay the onset of dural puncture headache rather than to prevent it altogether. It will be noted that there was no significant difference in the incidence of headache at 4 days postdelivery between the groups with and without epidural infusion. This observation has been reported previously and may reflect the increasing mobilisation which patients are allowed by day 4.[1] The small proportion of patients in whom blood patching was eventually considered necessary (five of 21) argues against the routine early use of the technique. However, when employed, blood patching was uniformly successful.

The need for prolonged hospital stay consequent upon dural puncture may have important implications for the individual patient, particularly if she already has other children at home, but is unlikely to represent an important burden on the provision of obstetric beds if the frequency remains as low as 1–2%.

Acknowledgment

The authors thank Miss G. Hall for typing the manuscript.

References

1. Crawford JS. *Principles and practice of obstetric anaesthesia*, 5th edn. Oxford: Blackwell Scientific Publications, 1984: 214–20.
2. Crawford JS. The prevention of headache consequent upon dural puncture. *British Journal of Anaesthesia* 1972; **44**: 598–600.
3. Crawford JS. Epidural drip and post-spinal headache. *British Journal of Anaesthesia* 1973; **45**: 1177.
4. Crawford JS. Experiences with epidural blood patch. *Anaesthesia* 1980; **35**: 513–5.
5. Brownridge P. The management of headache following accidental dural puncture in obstetric patients. *Anaesthesia and Intensive Care* 1983; **11**: 4–15.
6. Holdcroft A, Bevan DR, Morgan M. First year of an obstetric epidural service. *British Journal of Clinical Practice* 1974; **28**: 238–41.
7. Casey WF. Epidural test doses in obstetrics. *Anaesthesia* 1985; **40**: 597.

8. Kumar CM, Dennison B, Panchal HI. Epidural test dose. *Anaesthesia* 1985; **40:** 1023.
9. Shah JL. Epidural test doses in obstetrics. *Anaesthesia* 1985; **40:** 1131.
10. Mallaiah S. Epidural test dose. *Anaesthesia* 1986; **41:** 334.
11. Prince GD, McGregor DG. Epidural test dose in obstetrics. *Anaesthesia* 1986; **41:** 654–5.
12. Wilton NCT. Test doses for epidural analgesia—are we fooling ourselves? *Anaesthesia* 1986; **41:** 765–6.
13. Crawford JS. The strange case of the (inadvertent) continuous spinal. *British Journal of Anaesthesia* 1974; **46:** 82.
14. Hartley M. The strange case of the inadvertent spinal. *British Journal of Anaesthesia* 1975; **47:** 420.
15. Ward CF, Osborne R, Benumof JL, Saidman LJ. A hazard of double-orifice epidural catheters. *Anesthesiology* 1978; **48:** 362–4.
16. Galloon S. Test doses in extradural analgesia. *British Journal of Anaesthesia* 1978; **50:** 304.
17. Rees GAD, Rosen M. Test-dose in extradural analgesia. *British Journal of Anaesthesia* 1979; **51:** 70–1.
18. Ravindran RS, Viegas OJ, Tasch MD, Cline PJ, Deaton RL, Brown TR. Bearing down at the time of delivery and the incidence of spinal headache in parturients. *Anesthesia and Analgesia* 1981; **60:** 524–6.

Anaesthesia, 1987, Volume 42, pages 1114–1129

Correspondence

Visibility of pharyngeal structures as a predictor of difficult intubation 1115
P. Charters, MD, MRCP, FFARCS, S. Perera, MB, BS and W.A. Horton, FFARCS
J.R.B. Young, FFARCS 1115
Ergometrine and bronchospasm 1115
H. Hill, MB, BS, BSc, I. Geraghty, FFARCS, A. Hughes, MB, BS, P.S. Sever, PhD, FRCP and M. Schachter, MRCP
Erroneous actuation of the pulse oximeter 1116
I. Norley, FFARCS
M.B. Taylor, FFARCS 1116
Resistance to cardioplegia 1117
C.D. Miller, FFARCS and J.R. Dougall, FFARCS
Improving the success rate of axillary block 1117
R. Martin, MD, FRCP(C) and R. Dumais, MD
Efficiency of heat and moisture exchangers 1117
D.A.B. Turner, FFARCS and E.M. Wright, BM, BCh
G.D. Lowe 1118
Humidification by filters 1119
A.P. Kent, FFARCS
J. Allt-Graham, FFARCS, J. Gallagher, FFARCS and J.E.M. Strangeways, FRCPath 1119
Heat and moisture exchangers 1120
J. Replyuk
Expiratory obstruction in a circle system 1120
R.P. Alston, FFARCS
Supine faints 1120
D.L. Paul, FFARCS and D.W. McKeown, FFARCS
Postoperative complications of dystrophia myotonica 1121
L.M. Aldridge, FFARCS
Treatment of accidental hypothermia with the Clinitron bed 1121
E.L. Lloyd, FFARCS
J. Miles, FFARCS and G. Thompson, FFARCS 1122
A problem with the Argyll tracheal tube 1123
R.P.F. Scott, FFARCS and I. Chapman
Hanging drop and extradural pressures 1123
M.S. McKinney, FFARCSI
Opisthotonos again 1124
A.E. Cameron, FFARCS
High frequency jet ventilation and arterial to end-tidal CO_2 difference 1124
K.B. Shankar, MD
Propofol infusion for coronary artery bypass surgery in a patient with suspected malignant hyperpyrexia 1125
J. Richardson, FFARCS
Propofol in a morbidly obese patient 1125
I.J. Kirby, FFARCS and E.C. Howard, FFARCS
Nasotracheal intubation: another approach 1126
S. Mehta, FFARCS
Evaluation of oxygen analysers 1127
C. Hunsley, MIMechE
P.G. Roe, MB, BS, C.K.G. Tyler, FFARCS and P.K. Barnes, FFARCS 1127
Intra-operative myocardial ischaemia 1127
R.M. Griffin, FFARCS
I. Davis, FFARCS 1128
Unattached inner coaxial tube 1128
P.J. Roberts, FFARCS
Arousal from propofol 1128
D.N. Hunter, FFARCS, A. Thornily, FFA(SA) and R. Whitburn, FFARCS

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

Only the name sticks.

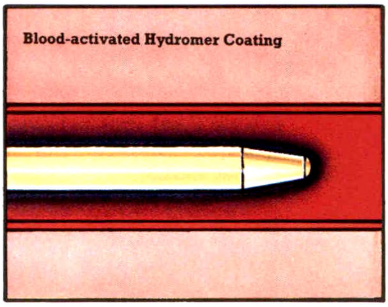
HYDROMER® is the special hydrophilic polymer that protects all HYDROCATH® catheters. When activated by body fluids it creates an aqueous complex which surrounds the catheter.

This complex reduces the surface friction of the catheter to less than that of wet glass, making insertion easier and reducing patient trauma.

Once in situ the Hydromer coat remains activated, creating a barrier at the blood/catheter interface.

For more information on the complete range of Secalon® Hydrocath central venous catheters please telephone (0793) 641791 or write to "Hydrocath", Viggo, P.O. Box 77, Swindon, Wiltshire, U.K.

® = Registered Trademark



Viggo

British Viggo
Faraday Road
Swindon
Wiltshire SN3 5HZ
Tel: 0793 641791
Telex: 444443 VIGGO G

BOC Health Care

Viggo International Sales
Chertsey Road
Windlesham
Surrey GU20 6HJ
Tel: 0276 77222
Telex: 859363 BOC GHQ G
Fax Nos: 0276 71333/77550

PHYSIO CONTROL

Physio-Control Ltd., Intec 2, Units 10-20,
Wade Road, Basingstoke RG24 0NE.
Tel: (0256) 474455 Telex: 858931 ELI EAG
Fax: (0256) 463770
A Lilly Medical Instrument Systems Company.

OUR GOAL: To take Pulse Oximetry that vital step beyond the known parameters.

OUR ANSWER: No ordinary oximeter, but one that combines continuous non-invasive monitoring with exacting new features.

Features such as a temperature compensated sensor that provides truly accurate results and a unique trend indicator to warn you of any short or long term changes. All this in an up-to-the-minute design with easy to view and read displays.

THE LIFESTAT® 1600 PULSE OXIMETER.

It's the one you've been waiting for.

Physio-Control and LIFESTAT are trademarks of Physio-Control Corporation. © 1987 Physio-Control Corporation.

Visibility of pharyngeal structures as a predictor of difficult intubation

We would like to comment on the study by Samsoon and Young (*Anaesthesia* 1987; **42:** 487–90) since we also have experience with the test [1,2] which forms the basis of their report. Mallampati's test scores the visibility of pharyngeal structures (faucial pillars, soft palate and uvula) in an attempt to predict difficult tracheal intubation. Three of us used this test as part of a pre-operative assessment in a study about tracheal intubation.

Samsoon and Young did not make it clear in their paper but they did not make the assessment in the way described by Mallampati. We also chose to examine our patients with 'the head in the neutral position' and the observer sitting 'opposite at eye level'. We graded patients class 1 to 3 as originally described because Mallampati did not describe a class where none of the soft palate was visible.

All three of us suggested independently that the test should be abandoned after a relatively short period because we considered that it was subjective and far too inconsistent in any given patient. The class 3 assessment (soft palate only visible) was found in 9/28 (32%) of patients by one of us and 4/32 (12.5%) by another. The third person involved, who is also a qualified dentist, exhausted his patience with the inconsistency of the test before a similar number of cases were documented. Only one of the 13 patients who were class 3 presented any difficulty at intubation; she had grade 3 laryngoscopy (tip of epiglottis only visible),[3] and for the remainder, the laryngoscopy was grade 1.

This information does not, of course, permit us to infer that the newly described class 4 (soft palate not visible) is not important. We did not, like Mallampati, recognise this category and suggest that Samsoon and Young need to be more precise about how it is defined (when limited to visual inspection). However, we can reasonably assume that the patients we recorded as class 3, would also be assigned similarly by these authors. Our experience does not allow us to agree with their contention that class 3 is a useful predictor of difficult intubation.

Royal Liverpool Hospital,
P.O. Box 17,
Liverpool L69 3BX

P. Charters
S. Perera
W.A. Horton

References

1. Mallampati SR. Clinical sign to predict difficult intubation (hypothesis). *Canadian Anaesthetists' Society Journal* 1983; **30:** 316–7.
2. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Freiberger D, Liu PL. A clinical sign to predict difficult tracheal intubation: a prospective study. *Canadian Anaesthetists' Society Journal* 1985; **32:** 429–34.
3. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39:** 1105–11.

A reply

Thank you for the opportunity to reply to this letter. The objective of our brief paper was to indicate that the less space there is between the posterior third of the tongue and the roof of the pharynx (which corresponds visually to loss of sight of pharyngeal structures), the greater is the likelihood of difficulty in visualising the laryngeal inlet.

Many anaesthetists who fulfill emergency commitments are relatively junior. If a test exists which suggests beforehand that there may be a difficulty, for example before embarking on a Caesarean section or on a laparotomy for intestinal obstruction, then, in our opinion, that anaesthetist will be alerted to possible problems. If the particular fear proves ill-founded (as, I agree, happens quite frequently), then at least the patient has not been placed at risk. One of our junior staff within the last few months used the test and refused to anaesthetise a patient without senior help. The author was the consultant who went to help and who failed to intubate the said patient using standard methods of induction for a patient for Caesarean section!

None of my colleagues finds any difficulty, inconsistency or boredom in undertaking the test.

St. Mary's Hospital,
Portsmouth

J.R.B. Young

Ergometrine and bronchospasm

It has been reported that bronchospasm may follow administration of ergometrine (ergonovine) in clinical practice.[1–4] The mechanism of this effect is not established. However, Sakamoto and others [5] recently proposed, on the basis of studies conducted in isolated canine bronchi, that it is due to a direct action on bronchial smooth muscle and, further, that the effect may be due to the partial agonist activity of ergometrine at serotonin (5HT) receptors.[5] We investigated this possibility using isolated human bronchial smooth muscle. Human bronchus was obtained from lung removed at surgery from six patients who underwent pulmonary lobectomy for carcinoma of the lung. Samples of bronchus 3–5 mm in length (internal diameter 3–7 mm) were dissected free from surrounding tissue and studied as intact segments under a resting tension of 1 g by a conventional tissue bath technique.[6] Ergometrine maleate 10^{-9}–10^{-4} M was added cumulatively to the bath. Ergometrine, either in the presence ($n = 19$) or absence ($n = 3$) of indomethacin 10^{-5} M, a cycloxygenase inhibitor, failed to cause contraction in any preparation despite demonstrable contractions in response to histamine 1–3 × 10^{-6} M or carbachol 10^{-6} M. In some preparations a degree of tone was induced by histamine 10^{-6} M; ergometrine 10^{-9}–10^{-4} M still failed to produce contraction in these tissues and in several segments produced moderate relaxation.

These data do not support the hypothesis that ergometrine-induced bronchoconstriction is due to a direct action on bronchial smooth muscle in man. Furthermore, these results urge caution in the extrapolation of results from isolated tissue of other species to man.

St. Mary's Hospital Medical School,
Norfolk Place,
London W2

H. Hill
I. Geraghty
A. Hughes
P.S. Sever
M. Schachter

References

1. Sellers WFS, Long DR. Bronchospasm following ergometrine. *Anaesthesia* 1979; **34:** 909.
2. Crawford JS. Bronchospasm following ergometrine. *Anaesthesia* 1980; **35:** 397–8.
3. Talwar KK, Kothari SS, Bhatia ML. Bronchospasm following ergometrine testing for coronary spasm. *American Heart Journal* 1985; **109:** 1415.
4. Louie S, Krzanowski JJ, Bukantz SC, Lockey RF. Effects of ergometrine on airway smooth muscle contractile responses. *Clinical Allergy* 1985; **15:** 173–8.
5. Sakamoto Y, Krzanowski JJ, Lockey RF, Duncan R, Polson JB, Szentivanyi A. The mechanism of ergonovine-induced airway smooth muscle contraction. *Journal of Allergy and Clinical Immunology* 1986; **77:** 354–64.
6. Hooker CS, Calkins PJ, Fleisch JH. On the measurement of vascular and respiratory smooth muscle responses *in vitro. Blood Vessels* 1977; **14:** 1–11.

Erroneous actuation of the pulse oximeter

Clinical monitoring of arterial oxygen saturation with the pulse oximeter is increasingly popular.[1] A feature of the pulse oximeter which is not always noted, is the extreme sensitivity of the device to movement at the detector probe. Any situation, clinical or otherwise, that causes slight, rhythmical changes in the optical pathway is likely to be read and displayed by the oximeter. This can be demonstrated readily as follows, in this case using a Nellcor pulse oximeter.

Example 1 (non-clinical). The finger clip probe is placed around the drip chamber of a standard intravenous fluid administration set primed with crystalloid solution. The drops are counted by the oximeter and a saturation displayed (usually about 80%).

Example 2 (non-clinical). The finger clip probe is held open with nothing but air within the light path. Slight opening and closing movements at the hinge of the probe are counted by the oximeter and again a saturation is displayed.

Example 3 (clinical). An arm is rendered pulseless by inflation of a proximal blood pressure cuff above systolic pressure. The finger probe is applied and no pulse is detected by the oximeter. If the arm is now shaken gently in a rhythmical manner the oximeter counts the shakes and displays a saturation of approximately 90%. This demonstration casts doubt on the validity of use of the pulse oximeter during cardiopulmonary resuscitation, as employed by Narang.[2] In his report, Narang used a pulse oximeter during the resuscitation of an 11-month-old child, and reported oximeter pulse detection in phase with chest compressions, with a saturation of more than 90%. In this case movement artefact as a means of oximeter actuation was not considered despite reported whole body movement of the child synchronous with chest compressions.

It is possible to fool the pulse oximeter as described in the above examples. When the device is used, due consideration should be given to the risk of movement artefacts causing erroneous readings.

Frenchay Hospital,
Bristol BS16 1LE

I. Norley

References

1. Taylor MB, Whitwam JG. The current status of pulse oximetry. Clinical value of continuous noninvasive oxygen saturation monitoring. *Anaesthesia* 1986; **41:** 943–9.
2. Narang VPS. Utility of the pulse oximeter during cardiopulmonary resuscitation. *Anesthesiology* 1986; **65:** 239–40.

A reply

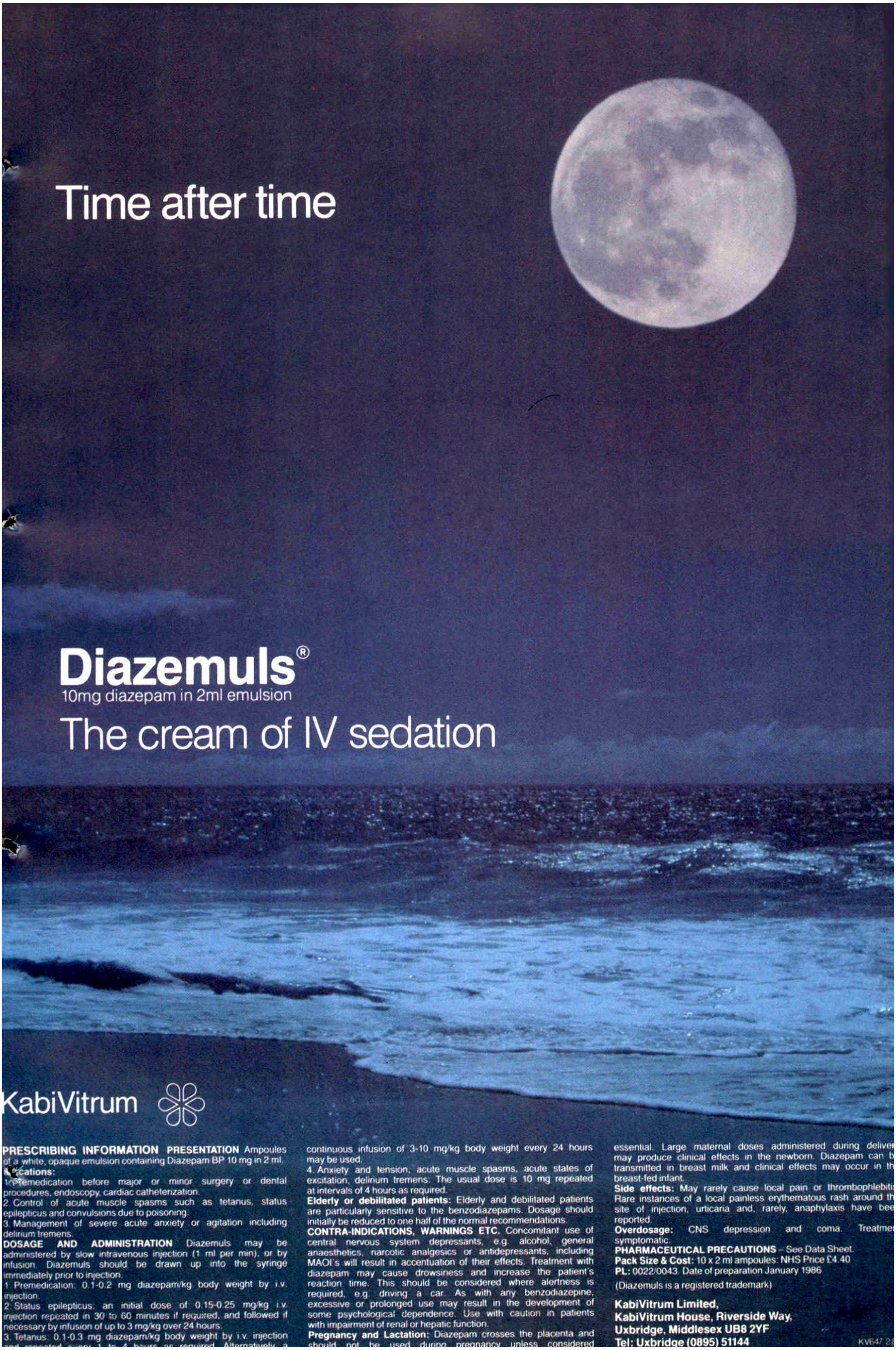
Dr Norley's letter illustrates that motion artefact is a possible source of error in pulse oximeter determination of arterial oxygen saturation. Anything, other than arterial blood flow pulsation, which causes modulation of the passage of light from light-emitting diodes to photodetector is a possible source of error. This, rarely, can be physiological, as in tricuspid regurgitation.

Motion artefact is reduced by pulse oximeters in the digital processing of the signal and by averaging the displayed arterial oxygen saturation over several seconds. This is effective in normal clinical usage but I have little experience of its use during resuscitation.

Pulse oximeters differ and, for example, it was not possible with a Biox 3700 to repeat the two non-clinical examples detailed above. Pulse oximeters which display the arterial plethysmographic waveform, in general have an advantage over those which display only the pulse amplitude of the signal, since this allows the operator to assess the quality of the signal from which the arterial saturation is derived and to observe any noise, such as motion artefact, which may alter its accuracy.

Hammersmith Hospital,
London W12 0HS

M.B. Taylor



PRESCRIBING INFORMATION PRESENTATION Ampoules of a white, opaque emulsion containing Diazepam BP 10 mg in 2 ml.

Indications:
1. Premedication before major or minor surgery or dental procedures, endoscopy, cardiac catheterization.
2. Control of acute muscle spasms such as tetanus, status epilepticus and convulsions due to poisoning.
3. Management of severe acute anxiety or agitation including delirium tremens.

DOSAGE AND ADMINISTRATION Diazemuls may be administered by slow intravenous injection (1 ml per min), or by infusion. Diazemuls should be drawn up into the syringe immediately prior to injection.

1. Premedication: 0.1-0.2 mg diazepam/kg body weight by i.v. injection.
2. Status epilepticus: an initial dose of 0.15-0.25 mg/kg i.v. injection repeated in 30 to 60 minutes if required, and followed if necessary by infusion of up to 3 mg/kg over 24 hours.
3. Tetanus: 0.1-0.3 mg diazepam/kg body weight by i.v. injection and repeated every 1 to 4 hours as required. Alternatively a continuous infusion of 3-10 mg/kg body weight every 24 hours may be used.
4. Anxiety and tension, acute muscle spasms, acute states of excitation, delirium tremens: The usual dose is 10 mg repeated at intervals of 4 hours as required.

Elderly or debilitated patients: Elderly and debilitated patients are particularly sensitive to the benzodiazepams. Dosage should initially be reduced to one half of the normal recommendations.

CONTRA-INDICATIONS, WARNINGS ETC. Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics or antidepressants, including MAOI's will result in accentuation of their effects. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. This should be considered where alertness is required, e.g. driving a car. As with any benzodiazepine, excessive or prolonged use may result in the development of some psychological dependence. Use with caution in patients with impairment of renal or hepatic function.

Pregnancy and Lactation: Diazepam crosses the placenta and should not be used during pregnancy unless considered essential. Large maternal doses administered during delive may produce clinical effects in the newborn. Diazepam can b transmitted in breast milk and clinical effects may occur in th breast-fed infant.

Side effects: May rarely cause local pain or thrombophlebiti Rare instances of a local painless erythematous rash around th site of injection, urticaria and, rarely, anaphylaxis have bee reported.

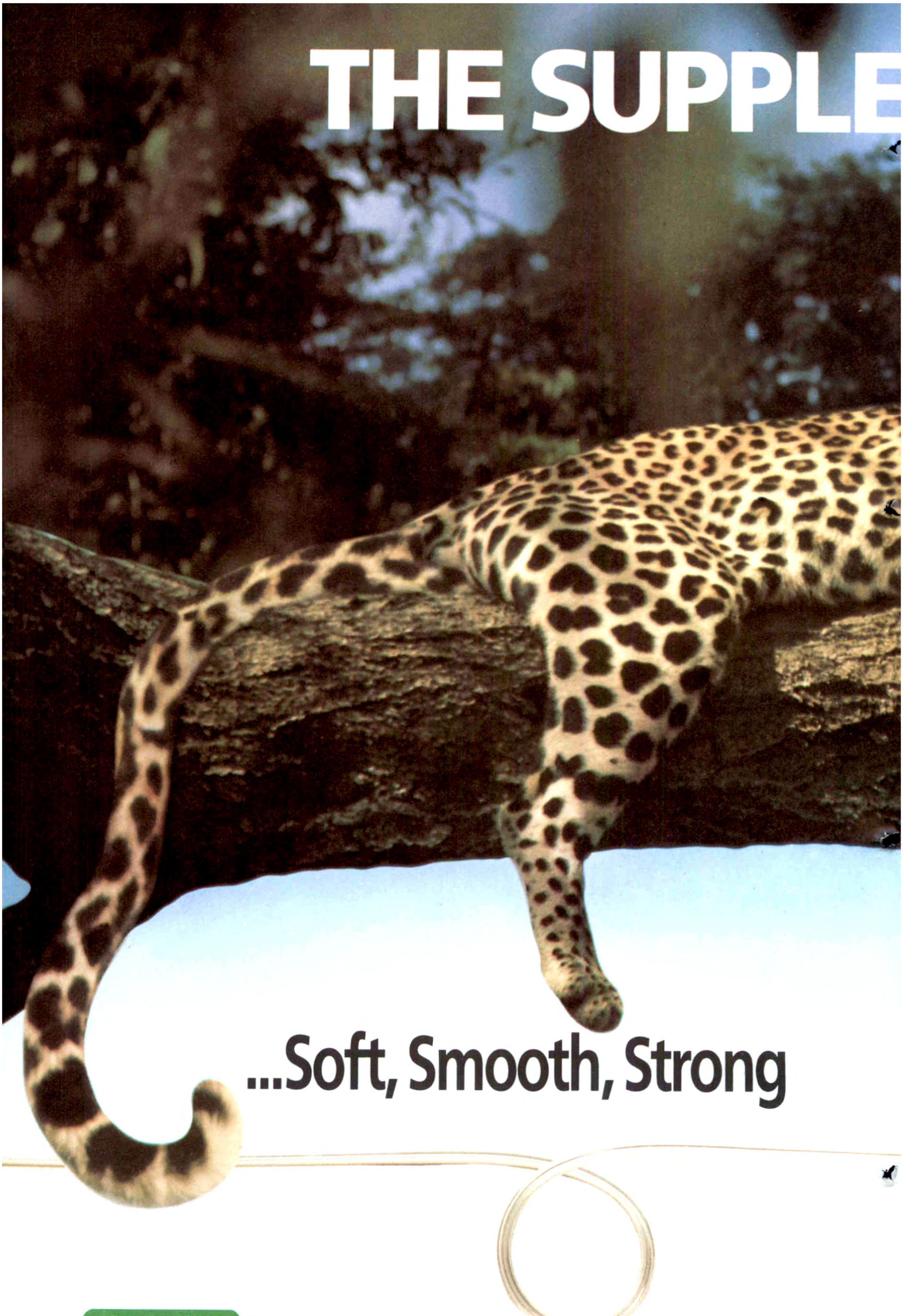
Overdosage: CNS depression and coma. Treatme symptomatic.

PHARMACEUTICAL PRECAUTIONS – See Data Sheet.
Pack Size & Cost: 10 x 2 ml ampoules: NHS Price £4.40
PL: 0022/0043. Date of preparation January 1986

(Diazemuls is a registered trademark)

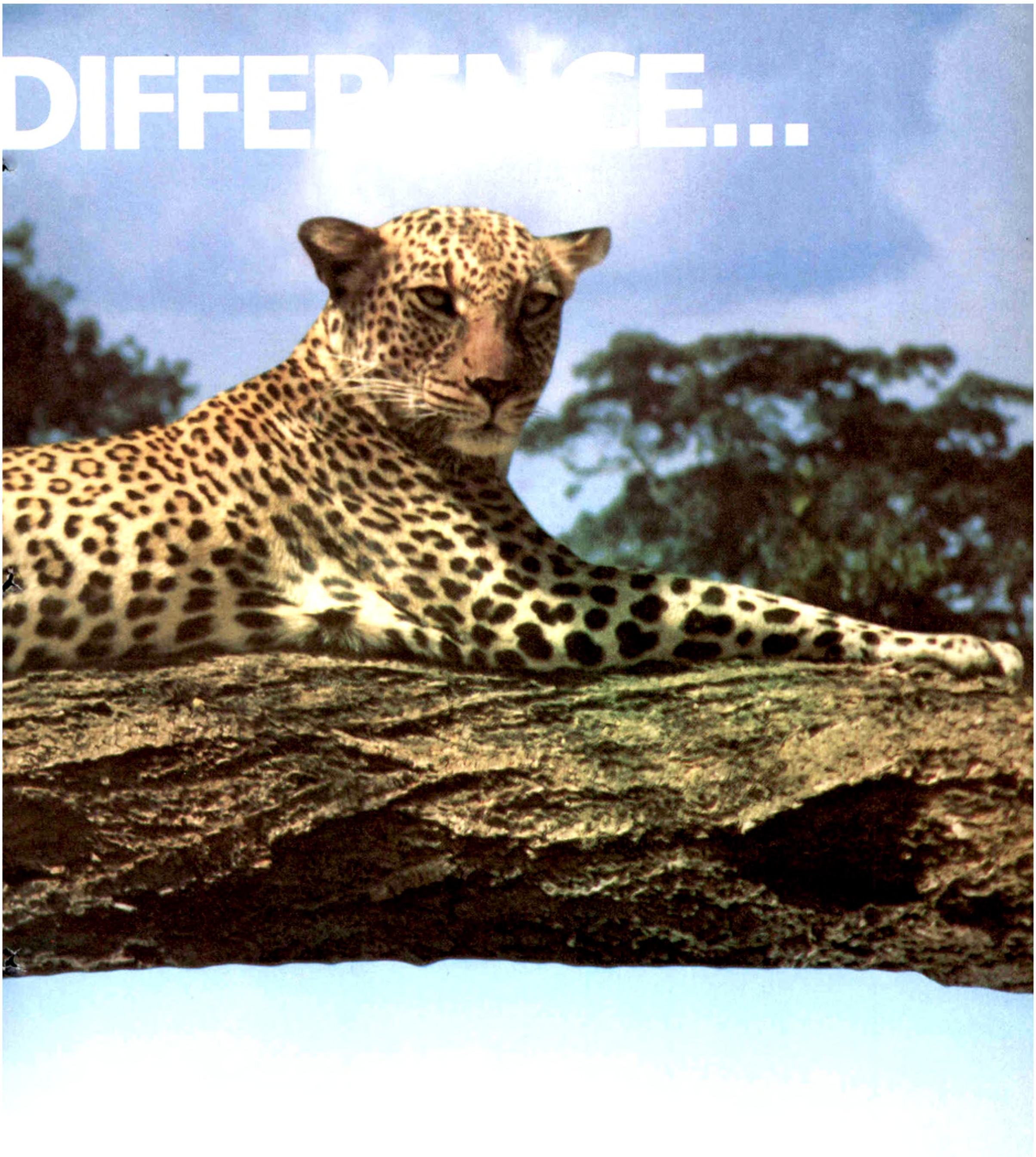
KabiVitrum Limited,
KabiVitrum House, Riverside Way,
Uxbridge, Middlesex UB8 2YF
Tel: Uxbridge (0895) 51144

KV647 2



VYGON

VYGON (UK) LIMITED



FLEXANE™

DEVELOPED TO OUTPERFORM ALL OTHER CATHETER MATERIALS

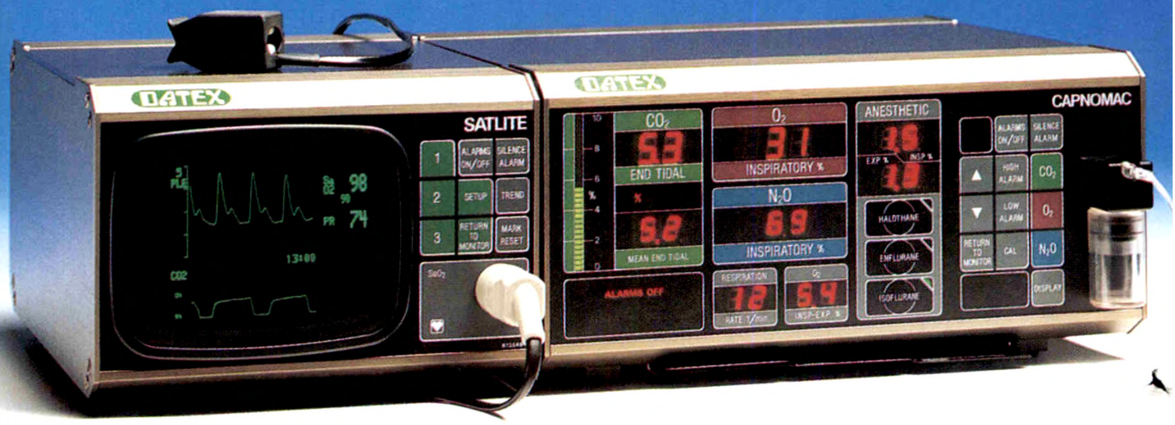
FLEXANE™ IS USED IN THE MANUFACTURE OF MULTICATH TRIPLE AND DOUBLE LUMEN CENTRAL VENOUS CATHETERS

FOR FURTHER DETAILS ON MULTICATH, COMPLETE AND RETURN THIS COU

VYGON VYGON (UK) LIMITED
BRIDGE ROAD, CIRENCESTER, GLOUCESTERSHIRE GL7 1PT
A

Name
Title
Hospital
Dept.
City

Pulse oximetry or multigas monitoring for your operating theatre? Why not both…



SATLITE™ and CAPNOMAC™

is an advanced operating theatre pulse oximeter providing SaO_2, pulse rate, the calibrated pulse waveform and trends of all three parameters.

is an anaesthesia agent and airway gas monitor, providing continuous breath-by-breath information on: CO_2, O_2, N_2O and the anaesthetic agent.

TOGETHER

they will provide you with the added bonus of the capnogram and trends of all the gases and the anaesthetic agent – both inspired and expired values.

See just how well SATLITE™ and CAPNOMAC™ together can meet your needs!

Distributed in the UK by:

For people who care

DATEX

Vickers Medical
Priestley Road,
Basingstoke,
Hampshire RG24 9NP, England
Tel. 0256 29141 Telex 858697

Resistance to cardioplegia

We wish to report an unusual case of difficulty in arresting the heart with cold cardioplegic solution.

A 62-year-old woman with angina and heart block, treated by unipolar endocardial pacing (Meditronic multiprogrammable pulse generator), presented for coronary artery surgery. A plastic occlusive drape (Johnson and Johnson) was stuck to the chest wall after induction of anaesthesia and skin preparation, and the pacemaker was taken from its infraclavicular pocket and laid on the drape. This insulated the pacemaker's casing from the patient and interrupted the circuit between the pacemaker and the patient's heart. Artificial pacing stopped and the patient's own pacemaker successfully took over control of her heart rate. Surgery continued uneventfully, the sternum was divided, the heart cannulated and, after aortic cross clamping, 500 ml of cold cardioplegic solution (St Thomas' Hospital) was infused rapidly into the aortic root. The heart stopped beating and the ECG tracing became isoelectric. However, this effect was short-lived and three additional boluses of cardioplegic solution (total 600 ml) were required over the next 10 minutes to keep the heart in asystole.

The heart was immobile after infusion of the third additional bolus of cardioplegic solution but electrical activity was still seen on the ECG monitor. Inspection of the pacemaker revealed that it was in contact with surgical drapes which were soaked in blood and saline and acted as an electrical pathway back to the patient. The pacemaker was electrically isolated from the patient by placing it inside a latex surgical glove and the ECG became isoelectric again. No more cardioplegia was required and the patient's surgery and postoperative course continued uneventfully.

The rapid return of electromechanical activity in this patient's heart may have been due partly to a failure of the cardioplegic solution to reach poorly perfused areas of her myocardium. However, these irritable foci were being inadvertently stimulated, and only when the circuit between the patient and her artificial pacemaker was interrupted did satisfactory cardiac arrest occur.

We recommend that great care is taken to ensure that the pacemaker is electrically isolated from the patient before the heart is arrested when a patient with an implanted pacemaker is to have cardiac surgery.

Western Infirmary, C.D. MILLER
Glasgow G11 6NT J.R. DOUGALL

Improving the success rate of axillary block

We read with interest the report by Tuominen *et al.* (*Anaesthesia* 1987; **42:** 20–2) which compared the success rates of axillary block with the perivascular and nerve stimulator techniques. We have a few years of experience at our institution of a nerve stimulator technique that we described at the Canadian Anaesthetists' Society meeting in 1985.[1] We locate all four components of the brachial plexus (radial, median, ulnar and musculocutaneous) using a pinpoint insulated needle. We usually use carbonated lignocaine 2% diluted to 1% in saline with adrenaline 1:200 000. We then inject three-quarters of the total dose at the sites of maximal stimulation of the two principal nerves responsible for the dermatome and myotome of the surgical site. The remaining quarter of the dose is reserved for the other two nerves. In our study we obtained a complete block in 90%, a partial block in 8.3% and a failure rate of 1.7%, in the hands of residents. We attribute the high success rate of this technique to the multicompartmental structure of the axillary sheath, as described by Thompson *et al.*[2] We therefore agree with the authors' conclusions but we consider that the success rate of the nerve stimulator technique can be further increased by selective isolation of all of the components of the axillary plexus.

Centre Hospitalier, R. MARTIN
Universitaire de Sherbrooke, R. DUMAIS
Fleurimont, Canada J1K 5N4

References

1. CUILLERIER DJ, MARTIN R, LÉNA P, LAMARCHE Y, BLACK R. Axillary block: a method to improve its success rate. *Canadian Anaesthetists' Society Journal* 1985; **32:** S71–3.
2. THOMPSON GE, RORIE DK. Functional anatomy of the brachail plexus sheaths. *Anesthesiology* 1983; **59:** 117–22.

Efficiency of heat and moisture exchangers

We wish to report the occurrence of inadequate humidification of inspired gas using a Pall Ultipor breathing system filter as a heat and moisture exchanger.

The patient was a 21-year-old man who developed respiratory failure secondary to pneumonia. His lungs were ventilated for 17 days with a tidal volume which ranged from 614 to 1070 ml and a minute volume between 6.3 and 10.4 litres, at an $F\mathrm{IO}_2$ between 0.5 and 0.98. His 9.0-mm Portex tracheal tube had to be changed on the 14th day because of partial obstruction

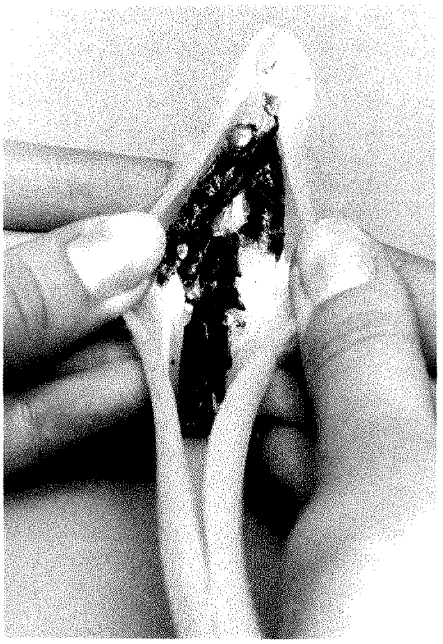


Fig. 1. The tracheal tube split open to show encrustations.

from dried secretions. A fibreoptic bronchoscopy performed at the same time revealed hyperaemic, bleeding tracheal mucosa. Figure 1 illustrates the dried secretions which had encrusted on the inside of the tracheal tube; this tube had not been changed during the previous 14 days. A Pall Ultipor breathing system filter was used throughout the admission to heat and humidify the inspired gas and was changed daily. Similar problems have not been experienced in this unit using hot water bath humidifiers.

An internal report about the performance of these filters[1] claims a water retention efficiency of 75%, which produces a level of humidification of inspired gas of 24 mg H_2O/litre at 25–31°C. This is greater than the Emergency Care Research Institute recommend for minimum heat and moisture exchanger output, namely, 21–24 mg H_2O/litre at 27–29°C for long-term ventilation. These data were obtained in a study that used a lung analogue with a tidal volume of 666 ml, peak inspiratory flow rate of 40 litres/minute and a frequency of 10 breaths/minute. Two independent studies[2,3] confirmed satisfactory humidification of inspired gas using this exchange. However, the data given for minute volumes in these studies reveal that values in the lower range of normal adult ventilation were used (6 and 7 litres).

Studies of the change in efficiency of heat and moisture exchangers (HME) following increases in tidal volume have been performed.[4,5] The efficiency of four types of HME was examined in one study and a significant decrease in efficiency of each HME was noted with increased tidal volumes and flows. For example, the efficiency of one HME was 61% using a tidal volume of 200 ml and a minute volume of 4 litres, but only 52% with a tidal volume of 700 ml and a minute volume of 14 litres.[4]

The patient discussed above received controlled ventilation of his lungs with large tidal and minute volumes. He was not atypical of patients ventilated on intensive care units in this respect. Heat and moisture exchangers offer many advantages that include reduction of bacterial infection, and convenience. However, in the light of our recent experience and the studies discussed above, their reliability as humidifiers on patients who require long-term ventilation with large minute volumes is unproven.

It should be noted that we have used over 200 of these filters over the past 3 months and this was the first tracheal tube blockage we have encountered. It may be that in patients who are ventilated at high minute volumes, small aliquots of physiological saline should be introduced into the trachea at frequent intervals. This may help to prevent the problem.

The Leicester Royal Infirmary,
Leicester LE1 5WW
D.A.B. Turner
E.M. Wright

References

1. Matkovich V. Performance of the Pall Ultipor Breathing System Filter as a heat and moisture exchanging bacterial filter. *Pall Technical Report BM 2080.* Pall Europe Ltd, 1985.
2. Chalon J, Markham J-P, Ali MM, Ramanathan S, Turndorf H. The Pall Ultipor breathing circuit filter—an efficient heat and moisture exchanger. *Anesthesia and Analgesia* 1984; **63:** 566–70.
3. Shelly M, Bethune DW, Latimer RD. A comparison of five heat and moisture exchangers. *Anaesthesia* 1986; **41:** 527–32.
4. Ogino M, Kopotic R, Mannino FL. Moisture-conserving efficiency of condenser humidifiers. *Anaesthesia* 1985; **40:** 990–5.
5. Hay R, Miller WC. Efficiency of a new hygroscopic condenser humidifer. *Critical Care Medicine* 1982; **10:** 49–51.

A reply

The Pall Ultipor breathing system filter is currently used by many intensive care units throughout Europe for long-term ventilation. A recent article (*Anaesthesia* 1987; **42:** 476–81) described the use of the Pall heat and moisture exchanging filter (HMEF) with 28 patients who required periods of mechanical ventilation for up to 22 days. The authors reported that the Pall HMEF performed satisfactorily as a heat and moisture exchanger in patients in need of long-term ventilation.

Our own test results on the performance of the Pall Ultipor breathing system filter showed a water loss from the test system of approximately 9 mg H_2O/litre at an exhaled gas temperature of 31°C. This result was obtained in a study that used a lung analogue with a tidal volume of 666 ml, peak inspiratory flow rate of 40 litres/minute and a frequency of 10 breaths/minute.

We also performed experiments at a tidal volume of 1000 ml, peak inspiratory flow of 50 litres/minute and frequency of 20 breaths/minute. Under these circumstances we measured a water loss of approximately 11 mg H_2O/litre. There is a small variation in water loss but the device still produces a level of inspired water vapour content in excess of the recommended minimum stated by the Emergency Care Institute, of 21–24 mg H_2O/litre at 27–29°C for long-term ventilation.

We would, therefore, not consider 1070 ml tidal volume and a minute volume of 10.4 litres/minute to be beyond the product's capabilities with regard to long-term ventilation.

Pall Medical Ltd,
Europa House,
Portsmouth PO1 3PD

G.D. Lowe

Humidification by filters

Dr Gallagher and colleagues, in their paper on the use of Pall Ultipor breathing system filters in long-term ventilation (*Anaesthesia* 1987; **42:** 476–81), seem to advocate their use as the sole means of airway humidification in patients whose lungs are ventilated artificially. There is, however, little detail revealed about the pulmonary pathology of the patients included in their study. It has been the experience on our unit that patients with large volumes of purulent pulmonary secretions do not receive adequate humidification from the sole use of a Pall filter: the secretions become increasingly solid and difficult to clear even with frequent saline irrigation and vigorous chest physiotherapy. Therefore, although a Pall filter is used for most of these patients on our unit, for the reasons discussed in Dr Gallagher's paper, we still return to a water-bath type humidifier for patients with severe pneumonia.

Walton Hospital,
Liverpool L9 1AE

A.P. Kent

A reply

Thank you for the opportunity to reply to Dr Kent's letter. We share many of the types of patients he describes but we do not share his difficulties with humidification using the Pall Ultipor breathing filter (PUBF). Our study focussed on the control of contamination of ventilators using the PUBF and did not include complete data on the respiratory pathology of these patients.

However, our experience using a PUBF as the sole means of humidification in adult patients whose lungs are ventilated artificially, now spans 2.5 years and over 200 patients who received controlled ventilation for periods of up to 70 days. These patients are drawn from an elderly South London population (mean age 66 years, 60% over 60 years) and are either medical admissions, mostly with respiratory disease, or major post surgical in a busy gastrointestinal hospital. The changeover to the use of the PUBF coincided with an impressive reduction in nosocomial related pneumonias in the intensive therapy unit (ITU), reduced periods of controlled ventilation and reduced mortality, although the use of retrospective data prevents definite conclusions. Bronchial toilet remains infrequent and difficulties with blocked tracheal tubes are rare.

We consider that the PUBF delivers adequate humidification and cited references in our paper, with the clear understanding that such passive devices cannot deliver 100% humidification to the tracheal air. Dr Kent will appreciate that a change from a water bath humidifier to a heat and moisture exchanger results in reduced sputum volume due to the removal of condensed water instilled in the airways. It is possible that such patients receive a reduced level of respiratory airway care unless nursing staff are aware of this difference. Consequently, we advise against the use of water bath humidifiers and heat and moisture exchanging filters within the same ITU for this reason as well as because of the risk of cross contamination.

We too practise frequent saline instillation as required and vigorous physiotherapy for patients with thick tenacious secretions, and prefer orotracheal tubes for ease of suction. We place emphasis on adequate systemic hydration and insist on a high standard of nursing care.

St. James' Hospital,
London SW12 8HW

J. Allt-Graham
J. Gallagher
J.E.M. Strangeways

Heat and moisture exchangers

Dr Shelly's article (*Anaesthesia* 1986; **41:** 527–32) describes the Siemens–Elema Servo Humidifer 150. We are very concerned about the statement that 'the Siemens–Elema Servo Humidifier has a fibreglass element'. The Siemens–Elema Servo Humidifier 150 insert consists of a hollow tube of cellulose sponge with an inner liner made of pure nylon felt. The Servo Humidifer 150 has never contained any type of fibreglass material as a component.

We appreciate the work that has been done by Dr Shelly's group in presenting the results of performance studies with five commonly used heat and moisture exchangers.

Siemens–Elema Ventilator Systems,
P.O. Box 94517,
Schaumberg,
Illinois, USA
J. Replyuk

Editor's note

The authors of the original article are sorry that they may have misled readers as to fact.

Expiratory obstruction in a circle system

Expiratory obstruction as a result of the presence of a foreign body in a Bain system was recently reported in this journal (*Anaesthesia* 1987; **42:** 564) and, after a similar personal experience with a circle system, some comment is required.

On examination of a circle system after two incidents, the protective cap from a Mix-O-Vial 125 mg ampoule of Solu-Medrone (Upjohn Ltd) was discovered impacted in the expiratory port of the absorber and was removed with difficulty. The diameter of the plastic cap was 22 mm. Fortunately, both patients made uneventful recoveries from anaesthesia. However, potentially fatal pulmonary barotrauma was possible. The first patient was protected by the development of a concomitant fault in the expiratory limb and the second patient was treated by rapid disconnexion. The real questions that arise from all these incidents are, however, who inserted the foreign bodies and why would they do this?

This report and that of Dr Jack demonstrate the potential dangers of a variety of inconspicuous objects found in theatre operating rooms, and that all untrained personnel should be made aware that they must not interfere with anaesthetic equipment. This report incidentally also emphasises the need for a more thorough method of testing circle systems before use. Employment of a bellows attached to the patient port has been recommended but pehaps a more simple and more readily applicable test is to breathe through the system oneself.[1]

Royal Infirmary,
9–16 Alexandra Parade,
Glasgow G31 2ER
R.P. Alston

Reference

1. Dorsch JA, Dorsch SE. *Understanding anaesthetic equipment*, 2nd edn. Baltimore: Williams and Wilkins, 1984.

Supine faints

Several people expressed surprise during a recent conversation in our department, at the notion that a person could faint while supine. An informal survey of anaesthetic colleagues showed that about half of those asked had neither seen such an event nor considered it to be a possibility. The following cases are typical of those reported to us, although these were witnessed by the authors.

A fit, 28-year-old man attended outpatients for routine cystoscopy. He was given no premedication and appeared to be anxious on arrival in theatre. He was placed supine on the cystoscopy table and a 23-gauge cannula was inserted with difficulty into the dorsum of his left hand. When the anaesthetist returned to the head of the table, the patient was found to be pale, pulseless, apnoeic and to have dilated pupils. The ECG showed a heart rate of less than 40 beats/minute. He was turned on his side, tilted head down and ventilated with 100% oxygen by facemask. He regained consciousness before atropine could be given and continued to be pale and sweaty for several minutes despite normal blood pressure and moderate tachycardia. After a rest of 10 minutes the patient underwent an uneventful general anaesthetic and cystoscopy, with normal recovery.

A fit, 23-year-old female was scheduled for a diagnostic laparoscopy as an outpatient. She was brought to theatre unpremedicated. An initial attempt at venepuncture was unsuccessful and, during a second attempt, another anaesthetist present noticed that the

Hespan*

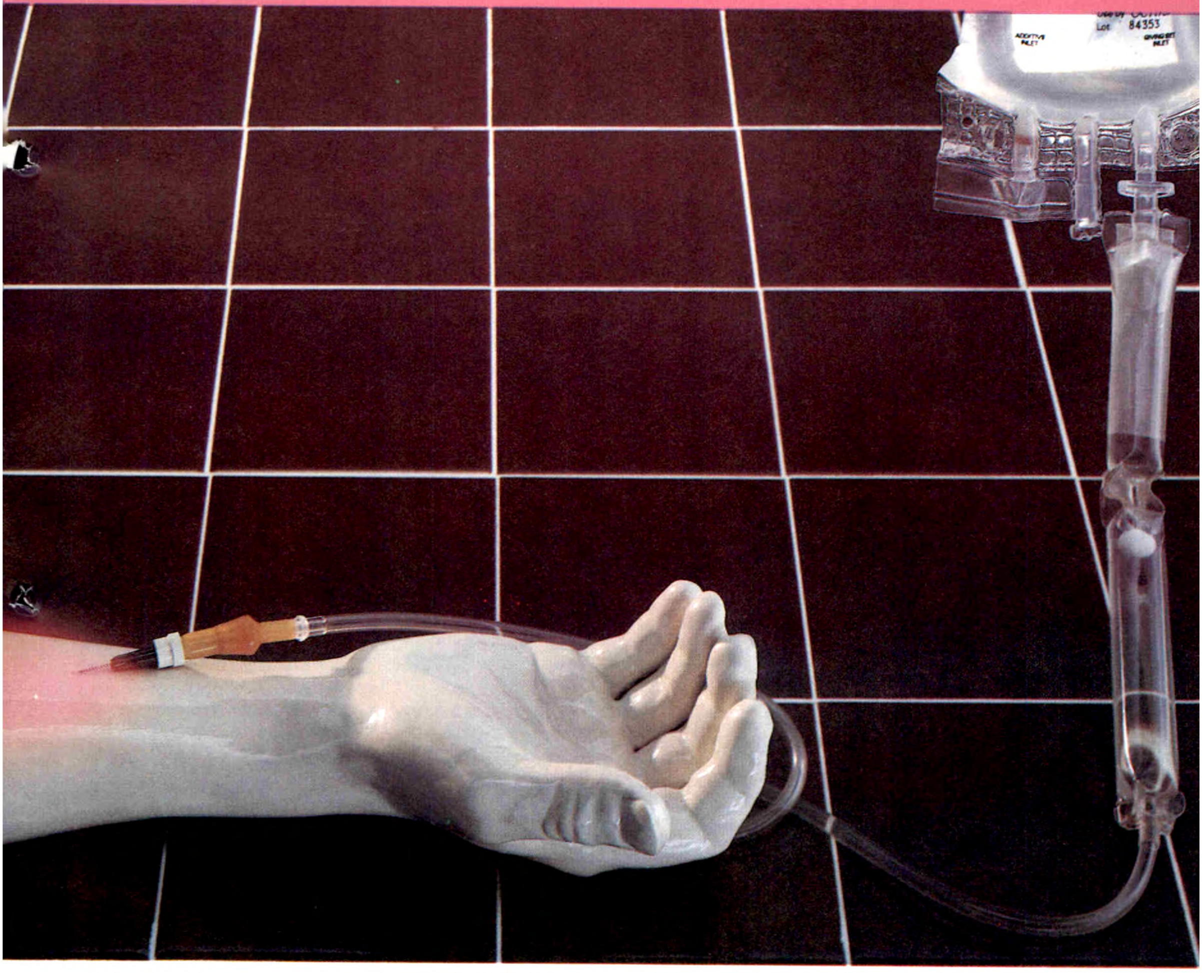
Hetastarch 6%

Controls plasma volume for a full 24 hours

Rapid plasma volume expansion restores cardiac output and tissue perfusion for vital organ function.[1-3]

Reliable increase in colloid osmotic pressure reduces the risk of tissue and pulmonary oedema.[4]

Available freely without dependence on blood donations, without the risk of transmitting disease.



References **1.** S. Lazrove, *et al., Crit. Care Med.*, 1980, *8(5).* **2.** V.K. Puri, *et al.* Data on file. **3.** V. Hempel, *et al., Anaesthetist,* 1975, *24,* 198-201. **4.** M.T. Haupt and E.C. Rackow, *Crit. Care Med.*, 1982, *10,* 159-162. For full prescribing information see next page. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel: (0438) 734549.

DU PONT

*Registered trademark

Hespan Prescribing Information

Composition Each 100ml Hespan contains: Hetastarch 6.0g. Sodium Chloride BP 0.9g. Water for injections BP qs, pH adjusted with Sodium Hydroxide. **Indications** 1. As a plasma volume expander in hypovolaemia. 2. Leucapheresis. 3. Extracorporeal circulation. **Contraindications Warnings** There are no absolute contraindications to the use of Hespan. Use with caution in patients with established renal failure. Hespan can produce dilutional effects on fibrinogen and prothrombin activity. In large volumes, Hespan may alter the coagulation mechanism and produce a transient prolongation of the clotting time. Use with caution in patients with severe bleeding disorders. Use with caution in patients vulnerable to vascular overloading. Caution should be observed before administering Hespan to patients with a history of liver disease in view of slightly raised indirect bilirubin levels observed on very rare occasions in volunteers. There is a low incidence of allergic reactions and the administration is not associated with raised plasma histamine levels. Mild periorbital oedema, urticaria or wheezing have been reported and are readily controlled by discontinuation of the drug and, if necessary, administration of an antihistamine. **Dosage and Administration—Plasma Volume Expansion** Intravenous infusion only, in an initial volume approximately equal to half the estimated blood loss. In adults the amount usually administered is 500ml to 1,000ml. Total dosage does not usually exceed 1,500ml per day or 20ml per kg of bodyweight for a typical 70kg patient, however the limiting dose will depend on circulating volume and haematocrit. In acute haemorrhagic shock, an initial administration rate approximately 20ml/kg/hr may be recommended, in burns or septic shock, it is usually administered at slower rates. **Leucapheresis** 250-700ml Hespan is typically added to the Y junction just above the bleed out in the ratio of 1 part citrated Hespan to at least 8 parts whole blood, ratios of 1:20 have been used. On rare occasions, 500ml Hespan has been infused into the donors 15-30 minutes before collection. Multiple leucapheresis procedures using Hespan of up to 2 per week or a total of 7-10 have been reported to be safe and effective. The safety of more frequent or a greater number of procedures has not yet been established. **Produce Licence Number** 2737/0042. **Package Quantities** Hespan is supplied in 500ml flexible plastic bags. Basic price £16.72. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel. (0438) 734549.

DU PONT

ANESTHESIA AND THE GERIATRIC PATIENT

Edited by
SUSAN WILSON KRECHEL, M.D.

Anesthesia and the Geriatric Patient represents the state of the art in the long-neglected area of anesthetic management of elderly patients. This new book features a collection of the most pertinent and informative topics on the subject. Approximately one-third of the book is devoted to basic science topics on physiology and pharmacology of aging as related to anesthesia practice with the remainder focusing on clinical aspects.

1984, 272pp., $44.50/£37.50
ISBN: 0.8089.1661.0

CLINICAL FEATURES IN ANESTHESIOLOGY

Edited by
JONATHAN L. BENUMOF,
University of California,
San Diego School of Medicine.

A Volume in the ANESTHESIA UPDATE Series

Covering the entire scope of anesthesia from both clinical and basic science perspectives, this comprehensive work presents the latest important developments in anesthesiology. With a concise emphasis on what is really "new" in the field, individual chapters by well-known experts discuss such vital issues as: • recent developments and breakthroughs in pharmocology • anesthesia techniques in operative, pre- and postoperative environments • special topics in the evolution of anesthesia, including a history of anesthesia and future directions • drug abuse in the medical profession.

1983, 288pp., $39.50/£33.00
ISBN: 0.8089.1580.0

Grune and Stratton
ORLANDO, FLORIDA 32887, U.S.A.
24-28 Oval Road, London NW1 7DX,
England

patient was pale and had a bradycardia (40 beats/minute). She became unresponsive to voice or shaking. She was placed head down and rapidly regained consciousness although she remained cold and sweaty with a bradycardia. A small dose of propofol (20 mg) was injected and she became relaxed and comfortable. She underwent an uneventful diagnostic laparoscopy (propofol, oxygen, nitrous oxide, enflurane) apart from a transient bradycardia on peritoneal puncture with the trochar.

A fit, fasted 25-year-old male volunteer, with a history of fainting, presented for an infusion study. He was approached with a large intravenous cannula while he lay supine. He became pale, sweaty and unrousable, with a slow, barely palpable pulse. He was turned onto his side and given oxygen before he regained consciousness about a minute later.

All three patients had a history of emotional faints and were noticeably anxious. Each faint occurred at the time of venepuncture and was followed by a rapid, uneventful recovery. Fainting outside hospitals is a common, usually benign event. However, it has been described as the cause of near misses and death during dental anaesthesia especially when it coincides with the induction of anaesthesia or occurs in the sitting position.[1–4] Fainting can undoubtedly occur while supine and, if unnoticed, may lead to asphyxia and death. It is also possible that the loss of consciousness and bradycardia may lead to the inappropriate instigation of full cardiopulmonary resuscitation. Most faints can be managed quite adequately by a head-down tilt, with maintenance of the airway and administration of oxygen. Intravenous atropine will speed recovery in some cases. Recurrences may be avoided with small doses of atropine or intravenous sedation.

The complications of fainting can be avoided by awareness and anticipation of the event and by rapid diagnosis and appropriate treatment when it does occur.

Royal Infirmary,
Edinburgh EH3 9YW
D.L. Paul
D.W. McKeown

References

1. Bourne JG. A dental-anaesthetic death. *Lancet* 1966; **1:** 879–80.
2. Bourne JG. Deaths with dental anaesthetics. *Anaesthesia* 1970; **25:** 473–81.
3. Shafto CE. Continuous intravenous anaesthesia for paediatric dentistry. *British Journal of Anaesthesia* 1969; **41:** 407–16.
4. Verrill PJ, Aellig WH. Vasovagal faint in the supine position. *British Medical Journal* 1970; 4: 348.

Postoperative complications of dystrophia myotonica

The recent report (*Anaesthesia* 1987; **42:** 529–33) was interesting. The authors indicated that the reported patient exhibited many of the intercurrent problems and postoperative complications of the disease. Myotonia was not precipitated by the administration of suxamethonium but it was stated that the use of the drug might have been avoided had the diagnosis been established at the time of operation. A review of the literature indicates that suxamethonium may precipitate severe myotonia to the extent that tracheal intubation is difficult or impossible. The use of the drug must be considered to be positively contraindicated when the diagnosis is known. This problem, together with the other hazards of anaesthesia in myotonic dystrophy, was reviewed elsewhere.[1] In this paper three patients, in common with the case reported by Drs Moore and Moore, were diagnosed after postoperative complications and the problems of anaesthesia in the undiagnosed symptomatic myotonic were specifically addressed.

Royal Infirmary,
Edinburgh EH3 9TW
L.M. Aldridge

Reference

1. Aldridge LM. Anaesthetic problems in myotonic dystrophy. A case report and review of the Aberdeen experience comprising 48 general anaesthetics in a further 16 patients. *British Journal of Anaesthesia* 1985; **57:** 1119–30.

Treatment of accidental hypothermia with the Clinitron bed

It is a pleasure to congratulate Drs Miles and Thompson (*Anaesthesia* 1987; **42:** 415–8) on their successful rewarming of the two patients described, although I disagree with their conclusion which implies that the Clinitron could safely be adopted generally for rewarming elderly patients.

Surface rewarming has been associated with many problems and elderly hypothermic patients are notoriously difficult to rewarm safely.[1,2] However, the report does support the contention that all hypothermic patients, including the elderly, should be rewarmed in an intensive care unit (ICU)[2–9] and, in fact, many of the measures used in these cases can only be used in an ICU. The report also provides support for the view that provided a patient is in an ICU, the actual method used for rewarming is unimportant.[2–5]

The inhalation of warm humidified gases is really neither an invasive procedure nor does it require specialised skills. The equipment, which is more widely available than a Clinitron bed, can be and is used by nonmedical personnel in the mountains and underground in caves.[2] In a study of 135 cases the inhalation of warm humidified gases was shown to be a very safe method of rewarming[10] with many physiological benefits,[2] though caution is still advised in the elderly except in an ICU.

The report emphasises that there was no afterdrop of core temperature in these cases but there is growing evidence that the afterdrop is an unimportant phenomenon[2,11–13] which bears no relation to the cause of death. Death is probably due to an imbalance between the size of the vascular bed and the circulating volume,[2,14] which may be too little or too large.[2]

This letter does not imply criticism of the work, but merely that the credit for the successful outcome has been applied wrongly. The credit should go to the skills of the staff in the ICU, including Drs Miles and Thompson, and not to an item of equipment.

Princess Margaret Rose Hospital,
Edinburgh EH10 7ED
E.L. Lloyd

References

1. Duguid H, Simpson RG, Stowers JM. Accidental hypothermia. *Lancet* 1961; 2: 1213–9.
2. Lloyd EL. *Hypothermia and cold stress*. London: Croom Helm, 1986.
3. Mills WJ. Accidental hypothermia: management approach. *Alaska Medicine* 1980; 22: 9–11.
4. Mills WJ. Accidental hypothermia. In: Pozos RS, Wittmers LE, eds. *The nature and treatment of hypothermia.* Minneapolis: University of Minnesota Press, 1983: 182–93.
5. Paton BC. Accidental hypothermia. *Pharmacology and Therapeutics* 1983; 22: 331–77.
6. Ledingham IMcA, Mone JG. Treatment of accidental hypothermia: a prospective clinical study. *British Medical Journal* 1980; 1: 1102–5.
7. Treating accidental hypothermia. *British Medical Journal* 1978; 2: 1383–4.
8. Braun P. Pathophysiology and treatment of hypothermia. In: Rivolier J, Cerretelli P, Foray J, Segantini P, eds. *High altitude deterioration*. Basel: S. Karger, 1985: 140–8.
9. Dubas F. Aspects medicaux de l'accident par avalanche: hypothermie et gelures. (Medical aspects of avalanche accidents: hyopothermia and frostbite.) *Zeitschrift fur Unfallchirurgie Versicherungsmedizin und Beraufskrankheiten* 1980; 73: 164–7.
10. Miller JW, Danzl DF, Thomas DM. Urban accidental hypothermia: 135 cases. *Annals of Emergency Medicine* 1980; 9: 456–61.
11. Golden FS, Hervey GR. The mechanism of the afterdrop following immersion hypothermia in pigs. *Journal of Physiology* 1977; 272: 26P–7P.
12. Golden FS, Hervey GR. The 'after-drop' and death after rescue from immersion in cold water. In: Adams JN, ed. *Hypothermia ashore and afloat*. Aberdeen: Aberdeen University Press, 1981: 37–56.
13. Savard GK, Copper KE, Veals WL. Possible mechanisms for the afterdrop of core temperature upon rewarming from mild hypothermia. *Presentation at Sixth International Symposium on Circumpolar Health, May 13–18, 1984, Anchorage, Alaska. Abstracts: 77.*
14. Golden FS. Problems of immersion. *British Journal of Hospital Medicine* 1980; 23: 371–83.

A reply

Thank you for the opportunity to reply. We are delighted that Dr Lloyd, with his extensive experience of hypothermia, has shown interest in our report. We should like to point out that despite often quoted problems with rapid external rewarming, heated baths and heated torso cradles are used successfully in the elderly.[1,2]

The inhalation of warm humidifed gases is certainly the least invasive of the central rewarming methods. It is an excellent option in an emergency, especially in cold ambient temperatures. However, the rate of rewarming is unpredictable in the spontaneously breathing patient and may be quite slow due to the depressed respiratory minute volume.[3–5] Prolonged hypothermia may be associated with a delay in diagnosis of any underlying disorder[2] and an increased incidence of complications.[1] We hope to have shown that the Clinitron bed provides a very steady and predictable rate of rewarming which allows physiological adjustment to the increasing body metabolic rate without the need for mechanical ventilation or significant inotropic support.

The bed is superior to any other method in terms of the patient's comfort and we wholeheartedly agree that it is desirable to conduct rewarming of severely hypothermic patients, where meticulous fluid balance monitoring is of the utmost importance, in an intensive care unit.

Royal Shrewsbury Hospital,
Shrewsbury
J. Miles
G. Thompson

References

1. Frank DH, Robson MC. Accidental hypothermia treated without mortality. *Surgery, Gynaecology and Obstetrics* 1980; 151: 379–81.
2. Ledingham IMcA, Mone JG. Treatment of accidental hypothermia: a prospective clinical study. *British Medical Journal* 1980; 1: 1102–5.
3. Slovis CM, Bachvarov HL. Heated inhalation treatment of hypothermia. *American Journal of Emergency Medicine* 1984; 2: 533–5.
4. Marcus P. Laboratory comparison of techniques for rewarming hypothermic casualties. *Aviation, Space and Environmental Medicine* 1978; 49: 692–7.
5. Harnett RM, O'Brien EM, Sias FR, Pruitt JR. Initial treatment of profound accidental hypothermia. *Aviation, Space and Environmental Medicine* 1980; 51: 680–7.

A problem with the Argyll tracheal tube

We have encountered a problem on two occasions with the Argyll low pressure cuff tracheal tube. We were unable to deflate the cuff at the end of the anaesthetic on the first occasion. On the second we were unable to inflate it during a routine pre-anaesthetic equipment check.

We cut the tracheal tube to a size appropriate for the patient, like most British anaesthetists, and subsequently ensure that the connector is firmly seated. Unfortunately, the latter procedure occasionally occludes the pilot tube to the cuff when a 9 mm i.d. tracheal tube is cut to about 22.5 cm in length (Figs. 1 and 2). This makes inflation and/or deflation of the cuff impossible.

We recommend that these 9 mm internal diameter tracheal tubes are not cut to less than 23 cm.

Southampton General Hospital,
Southampton SO9 4XY

R.P.F. Scott
I. Chapman

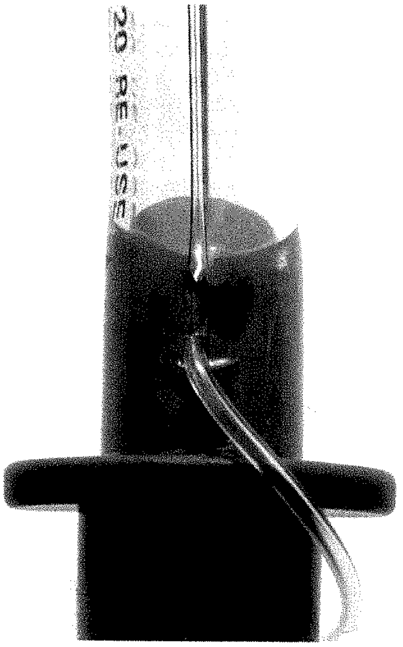


Fig. 1.

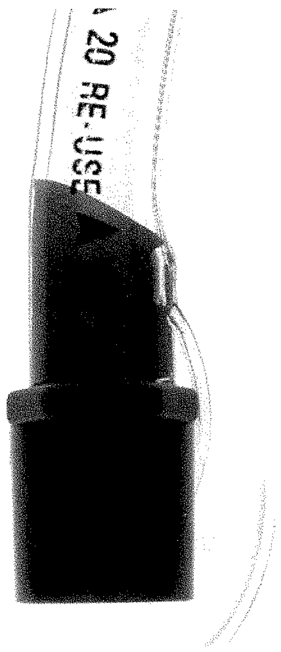


Fig. 2.

Hanging drop and extradural pressures

There has been much discussion recently over the genesis of the negative pressure in the extradural space. Some suggest that a continuous slight negative pressure exists in the extradural space when the spine is flexed;[1] other authors have postulated that the negative pressure is generated at the time of insertion of the Tuohy needle, either as a result of tenting of the dura[2] or, more recently, by a spring effect of the ligamentum flavum.[3]

It was the presence of this negative pressure that led Gutierrez[4] to describe the 'hanging drop sign' for location of the extradural space. There is another possible mechanism to account for this phenomenon, which may be of interest to other anaesthetists. This can be reproduced readily *in vitro*, using the needle from the Portex minipack.

The Tuohy needle, with stylet removed, is held horizontally or slightly tilted hub downwards and the tip is occluded to simulate the situation when the needle tip is in the spinal ligaments. A hanging drop (0.1–0.2 ml water or saline) can then be placed in the hub according to the usual method. When the occlusion at the tip of the needle is removed, simulating entry into the extradural space, the drop rapidly recedes into the needle.

This shows that the operation depends only on the removal of the occlusion from the tip of the needle and is independent of pressure levels due to any cause.

This process (which, presumably, is due to capillary action) may partly explain, but may further confuse the situation, since it does not explain why the hanging drop sometimes fails to indicate entry into the extradural space.

Altnagelvin Area Hospital,
Londonderry
M.S. McKinney

References

1. Odom CB. Epidural anesthesia. *American Journal of Surgery* 1936; **34**: 547–58.
2. Aitkenhead AR, Hothershall AP, Gilmour DG, Ledingham IMcA. Dural dimpling in the dog. *Anaesthesia* 1979; **34**: 14–19.
3. Zarzur E. Genesis of the 'true' negative pressure in the lumbar epidural space. A new hypothesis. *Anaesthesia* 1984; **39**: 1101–4.
4. Gutierrez A. Anestesia metamerica peridural. *Revista de Cirugia de Buenos Aires* 1932; **11**: 665–85.

Opisthotonos again

Dr A.E. Dingwall (*Anaesthesia* 1987; **42**: 565) reported violent writhing and opisthotonos in a 55-year-old female after anaesthesia for dilatation and curettage. The anaesthetic consisted of droperidol, alfentanyl, lignocaine and propofol. This reaction was thought to be an extrapyramidal side effect of the droperidol. However, it failed to respond to treatment with procyclidine.

This is a report of a further case of opisthotonos in a middle-aged woman who underwent dilatation and curettage and was anaesthetised with propofol. The patient was 44 years old and weighed 86 kg; she was short and therefore extremely obese. There was a 12-year history of epilepsy and she was treated with carbamazepine 200 mg four times daily. Other therapy consisted of bendrofluazide and iron. The electrolytes were normal. She gave a history of a cardiac arrest following diazepam presumably for treatment of a seizure.

In view of her gross obesity she was lightly premedicated with atropine 0.5 mg and pethidine 50 mg. Fentanyl 0.05 mg was given in the anaesthetic room followed by propofol 160 mg to which about 20 mg lignocaine was added. The patient's lungs were ventilated gently with nitrous oxide and oxygen via a facemask. Further doses of propofol 60 mg and 40 mg were given during the operation. The time from induction of anaesthesia to the end of operation was less than 10 minutes. Both operation and anaesthetic were straightforward and uneventful. The patient's condition was stable and unremarkable.

The patient appeared to behave normally on arrival in the recovery room and for the first half minute or so. She then abruptly became extremely restless with writhing athetoid movements of head, neck and limbs. An intermittent arching of her back was most marked, with outstretched lower limbs, so that her whole trunk was repeatedly thrown in the air. This impressive and intense activity continued for 20 minutes apart from a brief interruption when thiopentone 75 mg was administered. All movement, including respiration, ceased at the end of this time. Pulse and blood pressure were present and only slightly raised and, indeed, these gave no cause for concern throughout the whole episode. Quiet, regular breathing started after about 20 seconds. The patient was able to open her eyes on command after a further 20 minutes but still had occasional jerky movements of the limbs. A further 100 mg thiopentone was given carefully some 15 minutes later in an attempt to suppress this activity.

She was examined by the medical registrar who noted marked nuchal rigidity and increased tone and weakness on the right side. This weakness was present pre-operatively and it was difficult to assess whether deterioration had occurred. She was considered to be in a postictal state and was kept under close observation. Five hours later she had a grand mal seizure which lasted 5 minutes and responded to diazepam 2.5 mg. Phenytoin was added to her treatment. Further recovery was uneventful and she was able to go home on the second postoperative day with an early appointment to see the neurologist whom she normally attended.

The above sequence of events might seem to represent no more than a simple case of a postoperative seizure in a known epileptic, yet that, in itself, is a rare event in my experience. The marked degree of opisthotonos and the possible association with propofol merit reporting.

Vale of Leven District General Hospital,
Alexandria G84 8EE
A.E. Cameron

High frequency jet ventilation and arterial to end-tidal CO_2 difference

The paper by C.J. Mason (*Anaesthesia* 1986; **41**: 1251–4) is interesting because it was shown that $Pa\text{CO}_2$ can be monitored by a single large breath end-tidal CO_2 tension, but may I be permitted to comment on the conclusion of the subject which is somewhat misleading.

From the data shown on page 1253, Table 2, it can be computed that the mean $Pa\text{CO}_2$ is 5.37 kPa (SEM

RPMS INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

University of London

COURSE IN OBSTETRIC ANAESTHESIA AND ANALGESIA

at
Queen Charlotte's Maternity Hospital
18–20 November 1987

Fee £125

WEDNESDAY 18 NOVEMBER 1987

The Mother

Treatment of the shocked obstetric patient	*Dr G Hanson*
Placental transfer	*Dr F Reynolds*
Physiology of pregnancy and the anaesthetist	*Professor J Whitwam*
Management of labour	*Mr C. Sims*

Maternal Catastrophes

Cardio-pulmonary resuscitation of the pregnant patient	*Dr G Rees*
Failed intubation	*Dr R MacDonald*
Pregnancy and pre-existing disease	*Dr M de Swiet*
Anatomy and physiology of the epidural space	*Dr M Morgan*
Guest Lecture: THE PLACE OF THE EPIDURAL BLOCK IN MODERN OBSTETRIC PRACTICE	*Dr J Selwyn Crawford*

THURSDAY 19 NOVEMBER 1987

The Sick Mother

Aspiration pneumonitis	*Dr H F Seeley*
Pre-eclampsia/eclampsia	*Dr C W G Redman*
Anaesthesia and pre-eclampsia	*Dr A P Rubin*
Disseminated intravascular coagulopathy	*Dr E Letsky*
Anaesthetic maternal death	*Dr T Thomas*

The Anaesthetist

Fluid balance in labour	*Dr L E S Carrie*
Control of gastric acidity	*Dr R Laishley*
Spinal anaesthesia for caesarian section	*Dr I Russell*
General anaesthesia for caesarian section	*Dr M Morgan*
Guest Lecture: EPIDURAL ANAESTHESIA FOR CAESARIAN SECTION	*Dr D D Moir*

FRIDAY 20 NOVEMBER 1987

The Baby

Assessing the condition of the fetus	*Mr P Steer*
Neonatal resuscitation	*Dr D R Harvey*
Anaesthesia and neonatal outcome	*Dr D Brighouse*
Hypoxia and the fetal brain	*Dr P R F Dear*
Anaesthesia for the sick or hypoxic fetus	*Dr B M Morgan*

The Analgesia

Complications of epidural block	*Dr S Rehor*
Assessment of the obstetric patient for analgesia	*Dr G O'Sullivan*
Effects of analgesia on labour	*Dr J Thorburn*
Guest Lecture: LANDMARKS IN THE DEVELOPMENT OF REGIONAL ANALGESIA IN OBSTETRICS	*Dr A Doughty*

REGISTRATION FORM

To be returned to:

Symposium Secretary,
RPMS Institute of Obstetrics & Gynaecology,
Queen Charlotte's Maternity Hospital,
Goldhawk Road, London W6 0XG
(Tel: 01–740 3904)

together with the registration fee of £125 (this includes the charge for coffee, lunch and tea). Cheques should be made payable 'Institute Trust Fund'.

A receipt will be sent as confirmation of booking and must be produced on attendance.

CAPITAL LETTERS PLEASE

A87.30 –
Receipt No:

I wish to attend the Course in Obstetric Anaesthesia and Analgesia from 18–20 November 1987 and enclose my registration fee of £125.00

Name: Prof/Dr/Mr/Mrs/Miss/Ms ....

Specialty and Grade: ....

Address: ....

....

....

Telephone No: ....

UNIVERSITY OF LONDON

ROYAL POSTGRADUATE MEDICAL SCHOOL

HAMMERSMITH HOSPITAL

in association with

JANSSEN PHARMACEUTICAL LIMITED

announces

"A SYMPOSIUM ON ANAESTHESIA FOR DAY CASE SURGERY"

THURSDAY 29TH OCTOBER 1987

0900 – 1630 hours

Stamp Lecture Theatre, Wolfson Institute
Royal Postgraduate Medical School
Hammersmith Hospital, Ducane Road, London

This symposium is intended particularly for Anaesthetists and others interested in the management of day case surgical units.

The following topics will be included in the programme:

– the set-up and management of day surgery units,
– cost implications and financial provisions of day surgery units,
– intravenous anaesthetic agents for day case surgery,
– regional anaesthetic techniques for day case surgery.

Chairmen and Speakers:

Professor J G Whitwam
Professor of Anaesthetics
Hammersmith Hospital, London

Mr P E M Jarrett
Consultant Surgeon
Kingston upon Thames

Professor R M Winston
Professor of Fertility Studies
Hammersmith Hospital, London

Mr P H Lord
Consultant Surgeon
Wycombe General Hospital

Dr H B J Fischer
Consultant Anaesthetist
Redditch

Dr J Hargreaves
Consultant Anaesthetist
Manchester

Dr R F Cookson
Assistant Medical Director
Janssen Pharmaceutical Limited

Professor R C N Williamson
Director of Surgery
Hammersmith Hospital, London

Professor P O Bridenbaugh
Professor of Anesthesia
University of Cincinnati

Dr T W Ogg
Consultant Anaesthetist
Addenbrookes Hospital, Cambridge

Barry Caulfield
National Provider Liaison Manager
BUPA

Dr J E Charlton
Consultant Anaesthetist
Newcastle upon Tyne

Sister S Penn
Barnet General Hospital

0.29), $P_{E'}CO_2$ (after a single large breath) is 5.15 kPa (SEM 0.30), and (a − E′)P_{CO_2} is 0.22 kPa (SEM 0.04). There is a significant difference, as stated by the author, between Pa_{CO_2} and $P_{E'}CO_2$ in the group of patients studied by him. Therefore, the conclusion derived by the author, 'in a small group of critically ill patients receiving high frequency jet ventilation, measurement of end-tidal CO_2 tension following a single large breath did not differ significantly from arterial CO_2 levels measured simultanously', is inappropriate and misleading. It might be inferred from this statement that institution of high frequency jet ventilation in critically ill patients leads to near perfect ventilation/perfusion matching which results in $P_{E'}CO_2$ approaching Pa_{CO_2} in all patients. This is not true. The (a − E′)P_{CO_2} value increases in critically ill patients and, with the institution of high frequency jet ventilation, there is an improvement of ventilation/perfusion matching which results in a reduced (a − E′)-P_{CO_2} difference (0.22 kPa, SEM 0.04 in the group studied by the author, with maximum value of 0.52 kPa). However, the correlation between Pa_{CO_2} and $P_{E'}CO_2$ (after a single large breath) is good ($r = 0.989$) and therefore $P_{E'}CO_2$ (after a single large breath) can be used to predict Pa_{CO_2} taking into consideration the arterial to end-tidal CO_2 difference as 0.22 kPa. There is a possibility that this difference could be zero during high frequency jet ventilation in patients with normal cardiorespiratory function, in which case the authors' conclusion would be valid.

Queen Elizabeth Hospital,
University of West Indies,
Barbados, West Indies
K.B. Shankar

Propofol infusion for coronary artery bypass surgery in a patient with suspected malignant hyperpyrexia

An anxious, 46-year-old heavy goods vehicle driver who weighed 70 kg, was to have a three-vessel coronary artery bypass graft. He had a strong family history of malignant hyperpyrexia (MH) but had received an (unknown) anaesthetic some years before. His sister died after pyrexia during an anaesthetic, and family screening had revealed another sister and two other close relatives who were sensitive. Unfortunately, his own MH status was unknown because he failed to report for muscle biopsy.

His treatment included atenolol and diltiazem. Coronary angiography with diazepam and local anaesthesia with lignocaine was uneventful. Premedication for bypass surgery was with intramuscular midazolam, and pre-operative monitoring included core temperatures. Induction was with papaveretum 0.75 mg/kg, etomidate 0.3 mg/kg and pancuronium 0.15 mg/kg.

Anaesthesia was maintained with a slow loading dose of propofol 2 mg/kg, followed by an infusion at 12 mg/kg/hour at first and then reduced to 3 mg/kg/hour over the course of 45 minutes. The infusion was stopped when the core temperature on bypass was 30°C, since hepatic metabolism was thought to be minimal. The same loading dose was given during rewarming, followed again by an infusion at 3 mg/kg/hour until 20 minutes before elective tracheal extubation on the intensive care unit. There was no evidence of MH during the procedure, cardiovascular stability was excellent without any inotropic support and there was no awareness.

There are no theoretical contraindications to propofol in malignant hyperpyrexia (personal communication, Dr R. Ellis) and as an infusion it provides excellent anaesthesia for coronary artery grafting during cardiopulmonary bypass (personal communication, Dr C.S. Goodchild). It is described here as an alternative approach to a formidable anaesthetic problem.

St. James' University Hospital,
Leeds
J. Richardson

Propofol in a morbidly obese patient

The use in clinical practice of 2,6-di-isopropylphenol in emulsion form (propofol) was first reported in 1984.[1] It was noted that patients who received propofol experienced rapid recovery from general anaesthesia, with an absence of any hangover effect. Pharmacokinetic studies[2,3] indicate that the relationship of whole blood propofol concentration versus time following a single intravenous injection of propofol 2.5 mg/kg, can be represented by a three-compartment model. Propofol is highly lipophilic and distributes rapidly from blood into tissues. Cockshott[4] reported two estimates of the initial volume of distribution as 41.3 litres (SE 13.0) and 39.2 litres (SE 5.7). The same author also reported estimates of the corresponding half-life as 2.9 minutes (SE 0.7) and 2.3 minutes (SE 0.2). Metabolism of propofol is by conjugation in the liver. Hence the three-compartment model corresponds to a rapid initial distribution from blood, a rapid intermediate phase and a slower final phase of metabolism.

The following is a report of the use of propofol in a morbidly obese 22-year-old woman who presented with menorrhagia and required dilatation and curettage. The patient was 1.55 m tall and weighed 152 kg.

She had previously been injured in a road traffic accident and this resulted in a below-knee amputation of her left left. It was anticipated at the pre-operative examination that tracheal intubation might be difficult, as also would intravenous placement of a 14- or 16-gauge cannula. Examination of the patient's back suggested that epidural or subarachnoid block would also be difficult and thus regional analgesia was not used.

Metoclopramide 10 mg and temazepam 20 mg were prescribed as oral premedication 2 hours before surgery. Venous access was secured on arrival in the anaesthetic room, with a 21-gauge Y-Can in a vein on the ventral aspect of the left wrist. Pre-oxygenation was performed for 4 minutes. An induction dose (as judged by loss of the eyelash reflex) of propofol 180 mg was administered and the patient allowed to breathe spontaneously a mixture of 33% oxygen and 66% nitrous oxide via a Mapleson A system. The duration of surgery was 12 minutes, during which three incremental doses of propofol 20 mg were given (3, 6 and 9 minutes after the induction of anaesthesia). The patient was turned into the left lateral position and allowed to breathe 100% oxygen once surgery was completed. She opened her eyes to verbal command 90 seconds later. The patient remained pink and well perfused peripherally throughout the procedure, and did not exhibit any limb movement in response to the stimulus of surgery. She was fully alert and orientated on arrival in the recovery area.

Many studies involving propofol have been reported over the last 3 years but the majority of these have been confined to patients of ASA grade 1 or 2, and of body weights in the range 50–95 kg. As yet, there have been no reports of the use of propofol in a morbidly obese patient. We had anticipated administering a standard induction dose of 2.0–2.5 mg/kg, i.e. 300–375 mg propofol. However, loss of eyelash reflex was obtained after 180 mg (1.18 mg/kg) and anaesthesia was maintained satisfactorily with incremental doses of 20 mg propofol. These dosages were rather less than expected but they are compatible with the findings of Briggs *et al.*[5] that induction of anaesthesia can be achieved in 25% of patients with a dose of 1.0 mg/kg of propofol. Redfern *et al.*[6] investigated the use of incremental propofol in minor gynaecological procedures and also noted that there was no clear relationship between the induction dose of propofol and the weight of the patient. The dose requirement of propofol perhaps relates more closely to the lean body mass, rather than the total body mass of fat.

We found that the use of incremental bolus doses of propofol was satisfactory in this case, and that the rapid recovery from anaesthesia was advantageous.

Walton Hospital,
Liverpool

I.J. Kirby
E.C. Howard

References

1. Nightingale P, Healy TEJ, Hargreaves J, McGuiness K, Kay B. Propofol in emulsion form: induction characteristics and venous sequelae. *British Journal of Anaesthesia* 1984; **56:** 808P.
2. Briggs LP, White M, Cockshott ID, Douglas EJ. The pharmacokinetics of propofol ('Diprivan') in female patients. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 58–9.
3. Kay NH, Sear JW, Uppington J, Cockshott ID, Douglas EJ. Disposition of propofol in patients undergoing surgery. A comparison in men and women. *British Journal of Anaesthesia* 1986; **58:** 1075–9.
4. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 45–50.
5. Briggs LP, Clarke RSJ, Dundee JW, Moore J, Bahar M, Wright PJ. Use of di-isopropyl phenol as main agent for short procedures. *British Journal of Anaesthesia* 1981; **53:** 1197–1201.
6. Redfern N, Stafford MA, Brooker J, Hull CJ. Incremental propofol for minor gynaecological procedures. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 127–8.

Nasotracheal intubation: another approach

The letters from Dr Wright (*Anaesthesia* 1986; **41:** 1057) and Drs Kuwelker and Lawler (*Anaesthesia* 1987; **42:** 442) prompt me to report a technique which has been designed not only to avoid damage to nasal passages and the cuff, but also to prevent internal soiling of the tube and bacterial contamination of the trachea.

A polyethylene glove finger is firmly anchored with a fine cotton thread over the tip of a 42-cm-long suction catheter of 3.3 mm (10Ch) external diameter. The glove finger is fitted over the tube bevel with the suction catheter emerging out of the proximal end of the nasotracheal tube. The tube is lubricated with aqueous jelly and extra jelly is applied to the protective device. Once the bevel end of the tube reaches the oropharynx the glove finger is removed through the lumen of the tube by a steady pull on the suction catheter. The glove finger is inverted, bringing the contaminated surfaces together as it emerges through the tube. Intubation then proceeds in the usual way, using Magill forceps if necessary. This technique has a further advantage of ensuring that the glove finger is not lost; this device will soon become available in the United Kingdom.

Two other devices have been described to achieve the same objectives, but these devices are rather cumbersome to use in practice. Drs Cardan and Vlad described a protective sheath for the nasotracheal tube.[1] The other device is like a polyethylene funnel which acts as a protective sheath for the tube. It is introduced through the nose and pulled through the mouth. This device is marketed by Unoplast in the United Kingdom.

Burnley General Hospital,
Burnley BB10 3HP
S. Mehta

Reference

1. Cardan E, Vlad J. Protective sheath for nasotracheal tube. *Anaesthesia* 1986; **41:** 675–6.

Evaluation of oxygen analysers

The evaluation of five fuel cell oxygen analysers by P.G. Roe *et al.* (*Anaesthesia* 1987; **42:** 175–81) was interesting and well presented, and particularly useful was the 5-year cost of the product with sensors.

One statement in the evaluation did cause concern and that is related to polarographic cells and their use with nitrous oxide. The references cited clearly show the early polarographic cells could confuse nitrous oxide with oxygen when the batteries were nearly exhausted. However, I can confidently confirm that the Critikon Oxychek Oxygen Analyser (which utilises a polarographic sensor) has a fixed polarising voltage to avoid interference from nitrous oxide. It is thus suitable for use in anaesthetic systems.

Interestingly, the 5-year cost of an Oxychek Oxygen Analyser competes very effectively with the monitors detailed in the study since the sensor has a replacement cost of £45.

Critikon,
Broadlands,
Sunninghill,
Ascot, Berks SL5 9JN
C. Hunsley

A reply

Thank you for the opportunity to reply to this letter. Our evaluation of five fuel cell oxygen analysers was conceived at a time when recent publications had cast doubts on the use of polarographic cells with nitrous oxide. Orchard and Sykes[1] found that the IMI 3300 produced inaccuracies which were independent of polarising voltage, and were a function of the electrode. Piernan *et al.*[2] did find errors with exhaustion of the batteries, as Mr Hunsley mentions. Cole,[3] after a study which included the Critikon Oxycheck, stated that, 'in polarographic analysers a systematic error attributable to nitrous oxide was found.' Closer inspection of the paper, however, reveals this error to be very variable among the variety of models tested and, in fact, the Critikon Oxycheck performed very well with a mean error of 0.65% (maximum 0.9%) oxygen in nitrous oxide. Cole included the Oxycheck as a recommended model for both intensive care and theatre use.

Our comments based upon the above work were intended to explain the reason for the interest which developed in fuel cells at that time, and not to dismiss current polarographic models. An evaluation of current polarographic analysers in general is timely since advances have obviously occurred since the studies cited.

Westminster Hospital,
London
P.G. Roe
C.K.G. Tyler
P.K. Barnes

References

1. Orchard CH, Sykes MK. Errors on oxygen concentration analysis: sensitivity of the IMI analyser to nitrous oxide. *Anaesthesia* 1980; **35:** 1100–3.
2. Piernan S, Roizan MF, Severinghaus JW. Oxygen analyzer dangerous—senses nitrous oxide as battery fails. *Anesthesiology* 1979; **50:** 146–9.
3. Cole AGH. Small oxygen analysers. *British Journal of Hospital Medicine* 1983; **29:** 469–71.

Intra-operative myocardial ischaemia

It is surprising, indeed, that in the study by Dr Davis on the use of intrathecal morphine in aortic aneurysm surgery (*Anaesthesia* 1987; **42:** 491–7), none of the patients showed any evidence of ST segment changes. Dr Davis emphasised the maximum intra-operative changes in rate–pressure product (close to 20 000) which occurred without changes in ST segments. Therefore, although the value of rate–pressure product as a predictor of myocardial ischaemia is unreliable,[1,2] one might have expected some patients to develop ischaemic ECG changes. It was suggested that the anaesthetic technique 'exerted some cardioprotective effect'. However, as noted by the author, previous studies in similar groups of patients have found an approximate 40% incidence of myocardial ischaemia.[3–5] Furthermore, the majority of episodes of myocardial ischaemia are likely to be missed[3,5] without computerised ST segment analysis. Could the absence of

ST segment changes represent a similar lack of detection? The truth probably lies somewhere between this hypothesis, and careful anaesthetic technique.

The London Hospital,
Whitechapel, London E1 1BB
R.M. Griffin

References

1. Barash PG. The rate–pressure product in clinical anesthesia: boon or bane? *Anesthesia and Analgesia* 1980; **59:** 229–31.
2. Lieberman RW, Orkin FK, Jobes DR, Schwartz AJ. Hemodynamic predictors of myocardial ischemia during halothane anesthesia for coronary-artery revascularization. *Anesthesiology* 1983; **59:** 36–41.
3. Roy WL, Edelist G, Gilbert B. Myocardial ischemia during non-cardiac surgical procedures in patients with coronary-artery disease. *Anesthesiology* 1979; **51:** 393–7.
4. Coriat P, Harari A, Daloz M, Viars P. Clinical predictors of intraoperative myocardial ischemia in patients with coronary artery disease undergoing non-cardiac surgery. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 287–90.
5. Griffin RM, Kaplan JA. Myocardial ischaemia during non-cardiac surgery. A comparison of different lead systems using computerised ST segment analysis. *Anaesthesia* 1987; **42:** 155–9.

A reply

Thank you for the opportunity to reply to Dr Griffin's letter.

His surprise at the lack of ST segment changes probably only just exceeded mine: in the discussion I described the result as 'unexpected'. Certainly my crude technology may have contributed: the CM5 traces were recorded at 12.5 mm/second during potentially critical parts of the procedure and were later compared visually or with calipers to the V5 trace on the pre-operative electrocardiogram. It is possible, too, that other factors contributed: among them are small numbers, high drop-out rate, fortunate patient selection, single-handed anaesthetist and, perhaps, a cardioprotective procedure. Nevertheless, Dr Griffin has undoubtedly identified the most likely cause: the design of the study was inadequate for the purpose.

It is salutary to reflect on what can be missed even when it is sought with care.

Worcester Royal Infirmary,
Worcester WR5 1HN
I. Davis

Unattached inner coaxial tube

A recent incident at our hospital when the inner tube of a coaxial system became kinked, prompted some thought on the matter.

The two main physical hazards of the breathing system are that obstruction follows kinking of the inner tube, and that disconnexion of the proximal (machine) end of the inner tube may not be noticed. Both of these hazards may be avoided by the expedient of removing the special connector at the patient end and replacing it with a simple 15-mm male/male connector. This leaves the inner tube lying free within the outer tube at the patient end. The inner tube would have to be approximately 5 cm longer than in the existing system.

The inner tube will kink only if it is firmly held at both ends; if its distal end is free, its natural resilience or applied gas pressure will straighten it, thus avoiding the first hazard. If the proximal end of the inner tube becomes disconnected, the present system retains the tube within the system and this makes fault diagnosis more difficult. The modification enables the inner tube to slide out during customary manipulation of the hoses; it thus makes the fault instantly obvious and avoids the second hazard.

The modification does not affect the hazard of tube dislocation when actually attached to the patient (as with the existing system). It may also increase the likelihood of inadvertent use of the system when the inner tube is missing but the usual checks should pick this up. The position of the outlet of the inner tube will not remain constant with respect to the outer tube and may vary by 2–3 cm with flexion of the tubing but does this really matter? This modification should not make much difference to the behaviour of the system and I will be interested in any comments which may be forthcoming.

Princess Alexandra Hospital,
Royal Air Force,
Wroughton,
Swindon,
Wiltshire SN4 0Q7
P.J. Roberts

Arousal from propofol

We would like to report some observations of female patients anaesthetised for short procedures using propofol. On five separate occasions, three of us experienced amorous advances from patients as they awakened.

On arousal following cystoscopy, one young lady embraced D.H. and attempted to pull him onto the trolley, enquiring 'Do you want to come to a party?'. Another patient bluntly stated 'I want you!'. The other two anaesthetists (A.T. and R.W.) recorded similar incidents of embraces and kisses and one incident of the patient questioning the recovery staff, 'He looks a nice man. Is he married?'.

Has anyone else noticed these effects, or is it just we anaesthetists at the Middlesex Hospital?

The Middlesex Hospital,
London W1N 8AA

D.N. HUNTER
A. THORNILY
R. WHITBURN

Anaesthesia, 1987, Volume 42, pages 1130–1135

Book reviews

Current European Anaesthesiology 1130
Edited by R.M. JONES, H. BERGMANN, J. LASSNER, J.C. OTTENI AND D. THOMSON
Physics for the Anaesthetist, 4th edn 1130
W.M. MUSHIN AND P.L. JONES
Diagnostic Methods in Critical Care. Automated Data Collection and Interpretation 1131
Edited by W.C. SHOEMAKER AND E. ABRAHAM
Practical Management of Pain 1132
Edited by P. PRITHVI RAJ
Anaesthesia Review 4 1132
Edited by L. KAUFMAN
Intensive Care. A Concise Textbook 1133
C.J. HINDS
Neurosurgical Anaesthesia and Intensive Care, 2nd edn 1133
T.V. CAMPKIN AND J.M. TURNER
1986 Yearbook of Anesthesia 1134
Edited by R.D. MILLER, R.R. KIRBY, G.W. OSTHEIMER, L.J. SAIDMAN AND R.K. STOELTING
Advances in Anesthesia, Vol. 4 1134
Edited by R.K. STOELTING, P.G. BARASH AND T.J. GALLAGHER
Companion to the FFARCS Part III 1135
C.F. CORKE AND I.J.B. JACKSON

Current European Anaesthesiology

Edited by R.M. JONES, H. BERGMANN, J. LASSNER, J.C. OTTENI AND D. THOMSON. Pp. 308. John Wiley & Sons, 1986.

This second annual compendium of scientific papers in anaesthesiology is made up of papers from 11 European countries, including the USSR and Poland. It contains a total of 168 separate papers, published in summary form only; each paper is coupled with a review. Seventy-nine individuals have served as reviewers, 34 of whom are from the United Kingdom. The subject matter ranges from high-powered pharmacology and pharmacokinetics to very clinical subjects, such as awareness during anaesthesia. Pharmacology, physiology, co-existing diseases, resuscitation and intensive care, equipment and monitoring, local and regional techniques, paediatric anaesthesia, obstetric anaesthesia and patient safety-related issues are represented by papers published during the past year in the European literature. There are also papers about teaching methodologies and their effectiveness. To this American reviewer, of special interest were numerous papers studying the pharmacology of drugs not yet available in the United States. The reviews are certainly not whitewashes. For example, one reviewer states, 'One feels that the investigation should have been conducted with a tighter protocol, and that it should have been reported in more detail and with more care.' This is not exactly uncritical. The problem with any compendium of summaries such as this, is that it is all too tempting for the reader to read the review of the paper and get whatever 'take-home' messages there are in the critique, rather than making the possibly more difficult attempt to digest the summary of the paper itself. This gives more credit than is due to the reviewers, who probably spent just a short while on each paper, as opposed to the authors, who dedicated much time and effort to production of these peer-reviewed scientific papers. Sometimes the reviews in this book are as long as the summaries, a fact which tends to reinforce the reader's natural tendency to place emphasis on the critiques.

Nonetheless, a few days' study of this book by someone determined to keep current in anaesthesiology, would reveal many subjects of interest, some of which would have to be investigated further, to be sure, but the serious reader would gain a great deal of current information in most areas of current interest in anaesthesiology. Another thing the serious reader gains from this book is a sense of the truly massive breadth and depth of knowledge that is now created and disseminated yearly in our specialty. As for the American reader, such as myself, this opportunity to appreciate what is going on in Europe is certainly valuable.

J.H. TINKER

Physics for the Anaesthetist, 4th edn

W.M. MUSHIN AND P.L. JONES. Pp. xii + 648. Blackwell Scientific Publications, 1987. £32.50.

It has never ceased to amaze the reviewer that most anaesthetists show a deplorable lack of understanding of the basic physical principles on which their practice is based. This is in spite of the fact that the majority must have obtained a high standard in physics at A-level. The first edition of *Physics for the Anaesthetist* set out in 1946 to correct this anomaly and did so in a brilliant text, beautifully illustrated, which gained the affection of anaesthetists all over the world.

The third edition appeared in 1963 and nearly a quarter of a century has elapsed before the production of this fourth edition. The contribution of the physicist has now declined and we read in the preface that Dr Epstein left the team and that Professor Mapleson gave 'occasional advice', although Dr Willis advised the authors both as anaesthetist and as a physicist.

Much of the book follows the tradition of the earlier editions, with a painstaking and detailed exposition of basic physical principles relating to matters of everyday application including gas cylinders, reducing valves, vaporizers and flow through tubes. New sections include a fundamental consideration of physical quantities and an introduction to the SI system, the structure of matter, humidity and a gentle dip into electromagnetic radiation, electricity and electronics, including a selection of analytical techniques which are based on physical principles.

The diagram featured on the cover of the book may cause some confusion. The graph shows the pressure in a cylinder being filled with nitrous oxide (Fig. 8.8) while the representations of the contents of the cylinders show no fluid level and look more like the emptying of an oxygen cylinder (Fig. 8.15).

It is perhaps reasonable not to include the subjects of computing and data storage and processing. However, if spectrophotometry is included, it is difficult to understand the omission of mass spectrometry and chromatography which are also based on physical principles and have no less application to anaesthetic practice. There seems to be nothing on fluidics, and there can be no doubt of its relevance to ventilator design. Nevertheless, in spite of these omissions, the book remains wonderful value for teaching the basic principles of physics to anaesthetists. It is written by anaesthetists for anaesthetists and communication barriers are conspicuously absent.

J.F. Nunn

Diagnostic Methods in Critical Care. Automated Data Collection and Interpretation

Edited by W.C. Shoemaker and E. Abraham. Pp. xii + 502. Marcel Dekker, Inc., 1987. $69.75 (USA/Canada), $83.50 (elsewhere).

This book is part of a series intended for cardiologists, although a very large part of it is relevant to the anaesthetist and any other person who works in the intensive therapy unit. The subtitle *Automated Data Collection and Interpretation* is rather misleading since, although on-line recording and analysis are described, a good deal of the material does not fall into this category. Approximately 80% of it concerns cardiorespiratory monitoring in its various aspects.

The book starts off with a short description of the evaluation of severity of illness (APACHE, injury severity score, Glasgow coma scale, etc.). This is followed by two very straightforward chapters on cardiac and respiratory monitoring.

Inevitably some of the systems referred to have been partly overtaken by events. This particularly relates to the emphasis which is placed on transcutaneous oxygen measurement. It is claimed that the data provided by such devices can indicate oxygen delivery but it is also recognised that they are both slow and insensitive in response to change. Many clinicians now consider that this system has been overtaken by the pulse oximeter, which is not described in this book.

Chapter 5 describes the present state of computerisation of ITU data. The emphasis here is on record keeping, with particular reference to cost-effectiveness evaluation. There is a detailed section on blood gas analysis which is essentially a standard biochemical review. It emphasises the importance of quality control and there is a helpful description of the effects of body temperature changes. There is no discussion of the influence which pK variability has on such results.

To the reviewer, two of the more helpful chapters concern ITU pharmacology. The first of these is a gentle introduction to the theory of pharmacokinetics which includes as an example the regulation of digoxin dosage and the recognition and treatment of digoxin toxicity. This is followed by a chapter on the monitoring of other commonly used drugs. Here again some of the information has been superseded; for example, there is a detailed description of the use of naloxone, which to all intents and purposes has been shown to be of experimental importance only. The chapter on sepsis is restricted almost entirely to an assessment of the significance of delayed cutaneous hypersensitivity. Those familiar with the work from Professor Ledingham's department will already be aware of the value of this investigation.

The book finishes with a straightforward description of the pathophysiology, monitoring and therapy of respiratory failure. It includes a summary of the crystalloid/colloid controversy and concludes with an entirely uncontroversial list of recommendations for treatment.

From the foregoing it will be apparent that the book does not contain very much that is new and, indeed, in many places it reads as a straight textbook of applied physiology. Each chapter is followed by an extensive and relatively up-to-date reference section. Because the total subject matter is restricted, the index is short, but quite adequate. The book is well produced and adequately illustrated. The price is what one has come to expect.

J.C. Stoddart

Practical Management of Pain

Edited by P. Prithvi Raj. Pp. xvi + 956. Colour plates. Year Book Medical Publishers, 1986. £120.00.

This book presents current US practice for the trainee pain specialist and the editor has employed 44 authors, about half of whom are anaesthetists. Dr Raj was involved as sole or co-author in half the chapters but his control as editor has apparently been slight. The strength of the modern pain clinic is the multidisciplinary approach and the results are usually excellent when experts write about their own specialised fields. This is not necessarily the case when they stray into less familiar pastures.

The book is divided into six sections but considerable duplication occurs and the emphasis given to different topics is often surprising. The 'failed surgical back' and arachnoiditis are allotted only a few lines, yet electromyography and chemonucleolysis receive over 12 pages each.

The first section, which deals with general considerations, contains useful reviews of epidemiology and American pain clinic organisation. Much of the remainder is waffle. The second section deals with physiology, evaluation and investigation of pain. Basic neurological examination (medical school standard) is spread over 44 pages, whilst psychological tests are dismissed in under two pages. A large subdivided chapter called 'Pain syndrome and rationale for management' contains very little that is not repeated later, except for two very neat reviews of central pain and spinal injury pain.

Postoperative pain starts the next section but most of the chapter is devoted to detailed descriptions of nerve blocks which are all repeated in later chapters by the same author. Much of the large chapter on obstetric pain relief is taken directly from Ostheimer's existing publications, sound though they are. A workman-like chapter on pain due to trauma covers the pathophysiology of acute pain. Following this Ferrer-Brechner presents an outstanding review of cancer-related pain. Interesting chapters on phantom limb pain and post-herpetic neuralgia highlight the huge gaps in understanding of the pathogenesis of many chronic pain conditions and also the paucity of controlled trials of treatment.

The next section, on regional pain, deals poorly with subjects such as orofacial pain, the neuropathies and back pain. Cervical pain and sympathetic pain are handled more satisfactorily. Part V is devoted to pharmacology and contains some stimulating contributions from Denson, Mather and de Jong.

The remaining 300 pages of text cover virtually all the current therapeutic techniques and consist mainly of detailed descriptions of how to perform nerve blocks. Most of the techniques and treatments are presented without any critical analysis or justification. Case reports are included, but add little convincing scientific weight to the argument. This is not the way to train pain doctors of the future. The section on neurosurgery, however, is particularly good and wisely emphasises a very cautious application of these procedures. Cryo-analgesia has its own chapter but radiofrequency neuroablation is barely mentioned. Acupuncture and transcutaneous electrical nerve stimulation are covered extensively, and (the beatification of the pain therapist may be imminent) acupuncture is recommended for, among other things, tonsillitis, impotence, schizophrenia and deafness. Psychological treatment methods and physical therapy are given only relatively brief consideration and this produces an unfortunate bias towards the invasive injection therapies.

The appendices (which include useful pharmaceutical recipes), the references, the index and the printing and layout are all very satisfactory. Unfortunately, the illustrations represent a serious flaw in this book. A mass of colour illustrations are herded together at the front of the book and, like many of the black and white photographs and X rays, are of poor quality and little consequence. Considerable repetition of illustrations occurs, even in adjacent chapters. Transatlantic language differences are apparent and the reader has to adjust to words such as biopsychosocial, skeletalgia and thanatology whilst, annoyingly, American brand names are often used for drugs. It is scandalous that the United States of America price of $125 should be transposed to £120 in the United Kingdom at the current rate of exchange!

This is a useful book which contains much that is very good. There are, however, some serious imperfections which firmer editorial guidance might have eliminated. Pain clinics and anaesthetic departments may wish to own a copy but many individuals will find the cost–benefit analysis unfavourable.

D.M. Justins

Anaesthesia Review 4

Edited by L. Kaufman. Pp. 234. Churchill Livingstone, 1987. £14.95.

The latest in this series will need little introduction to British *Anaesthesia* readership. The previous volumes have enjoyed considerable popularity.

Dr Kaufman's introduction states that special emphasis is placed on medicine applied to anaesthetic practice. Ignoring the fact that anaesthetic practice without medicine applied to it is mere technology, one applauds the chapter on the treatment of acute severe asthma (Hind and Robertson) and ponders why Davies and Camm needed two short, rather than one long, chapters to deal with anti-arrhythmic drugs (similarly, Sumner and James on paediatric anaesthesia and intensive care). After that I thought the book was mainly about anaesthesia.

D.C. White's piece on narcotics in general anaesthesia, with its extensive reference list, is a particularly good resource on that disparate topic. There are other chapters on high frequency ventilation, cardiac surgery and endocrine responses to surgery; these are useful but the material contained is easily retrieved elsewhere. Alternatively, Wainwright on anaesthesia and laser surgery impressed me.

A chapter on medicolegal aspects is hackneyed as an idea, although the author tries to be original. Using this chapter as a context rather than a target, I am concerned at the increasing number of our colleagues, some of them comfortably retired from practice, who pontificate on medicolegal matters with impunity at a time when the costs of medical defence seem to be out of control. As with this chapter, opinions unsupported by precedent or logical argument, abound. Standards of practice should be reached on the basis of experience and scientific reasoning, and not *ex cathedra* statements from medicolegal camp followers.

Dr Kaufman, unlike some editors of multi-author texts, does not hide modestly behind the scenes. Indeed, he is all over the book, often helpfully. One wonders if he would consider acting as continuity man, introducing each chapter with his view on the main points that emerge and his reason for selecting the topic in the first place. Apart from other benefits, it would allow reviewers a better idea of the real editorial policy with this series. As things stand, the contents of the present volume are neither related nor topical.

As a further example of the foregoing difficulty, the volume commences with a piece on ether anaesthesia at University College Hospital (140 years ago). There is nothing original here and one wonders why it is there at all. Of course this is the year when more and more of our colleagues are concentrating on less and less important matters in the history of anaesthesia to the point of risking sublimation or involution. I hope there was no unworthy thought on the part of the editor and publisher of this book, that they should get in on the act too!

A.A. SPENCE

Intensive Care. A Concise Textbook

By C.J. HINDS. Pp. 378. Baillière Tindall, 1987. £14.95 (paper).

Textbooks of intensive care have hitherto fallen into one of two types. There are the very large multi-author books, wide in their scope and containing an immense amount of detail. The other books are short and valuable to nurses. Sections on intensive care in anaesthetic books are often selective in their subject matter and uneven in detail. There has been a long-standing need for an introduction to intensive care medicine for doctors in training. Dr Hinds has written it.

The book begins with an introduction to the nature and problems of intensive care. Succinct accounts of cardiovascular and respiratory physiology and monitoring follow. Each body system is then dealt with chapter by chapter. The author follows a similar pattern for each system. There is an introduction which includes the relevant history; a review of the pathophysiology of the system's failure; the clinical features of this failure; investigation, management and monitoring; further reading and references.

Every chapter is concise, accurate and up to date. The clarity of the text is enhanced by good diagrams and illustrations. The references reveal the very considerable breadth of the author's reading but the essentials of intensive care medicine are encompassed in a single volume of less than 400 pages.

However, the order of the chapters is less systematic than their contents. The trainee will not follow easily the chapter on trauma without having read the later chapter on respiratory failure. It would have been better to discuss specific causes of respiratory failure and their management after discussing the general principles of the management of respiratory failure, including mechanical ventilation. It would also have been helpful if, after reviewing the treatment of each failing system, there was a more didactic summary of what to do. Someone of the author's experience need have no fear of doing this and trainees will look for it. This book is destined to become the standard bench book in intensive care units in the United Kingdom (and in many other countries too). Therefore, tables of normal values and drug doses would make quick reference easy.

However, these criticisms do not diminish the excellence of this book. It really is a concise textbook of intensive care medicine. Within a very short time it will become essential reading for candidates for the Part 3 FFARCS examination (and for their examiners). Doctors in other disciplines who want to learn about intensive care will find no better place to start. Those who have practised intensive care for many years will find it first-class revision and a valuable source of reference. Many tutorials and lectures will begin here. Dr Hinds has performed an outstanding service for doctors and patients alike; I hope that there will be many future editions.

J.F. SEARLE

Neurosurgical Anaesthesia and Intensive Care, 2nd edn

By T.V. CAMPKIN AND J.M. TURNER. Pp. 323. Butterworths, 1986. £40.00.

The first edition of Campkin and Turner's book was immediately accepted as a standard textbook on the specialised subject of neurosurgical anaesthesia and intensive care. The second edition does not fail to maintain this high standard. The book is conveniently divided into sections, the first of which is devoted to the physiology and pharmacology of the cerebral circulation and the intracranial effects of anaesthetic agents, and other relevant factors. Part 2, entitled 'Basic considerations', encapsulates in 70 pages the essentials of neurosurgical anaesthesia, and should be read by all candidates for the Part 3 FFA examination who are required to know the principles of neurosurgical anaesthesia. The attention to practical detail is admirable; the authors, while they report often conflicting literature studies, do not hesitate to emphasise what they believe to be important in the management of neurosurgical patients.

Chapters on anaesthesia for particular neurosurgical operations, including spinal surgery and paediatric neurosurgery, form the third part of the book. Again, the combination of wide academic information and careful attention to practical detail, imprinted with the authors' own authoritative views, make this an essential source of reference on the more specialised aspects of the subject.

The final section, on intensive care, emphasises the potential for improvement in the care of patients with head injuries. This section, if no other, should be read even by those who are not directly involved in neurosurgical anaesthesia, since it emphasises principles which are, very regrettably, often neglected in the management of these patients inside and outside neurosurgical units.

There are a number of excellent textbooks on neurosurgical anaesthesia but this has no equal. It apparently considers a very specialised field but the principles are applicable to many related aspects of intensive care, trauma and cerebral physiology and pharmacology. It is invaluable reading for candidates for postgraduate examinations in anaesthesia (including Parts 2 and 3 for the FFA) and for all anaesthetists who may be involved in the management of patients with immediate or incidental intracranial pathology of any kind, as well as a reference source for neurosurgical anaesthetists. Despite occasional small and uncharacteristic typographical errors the format and production are good and complement the value of this excellent book.

J.N. HORTON

1986 Yearbook of Anesthesia

Edited by R.D. MILLER, R.R. KIRBY, G.W. OSTHEIMER, L.J. SAIDMAN AND R.K. STOELTING. Pp. 387. Year Book Medical Publishers, Inc., 1986. £43.00.

Every year, when the new edition of the *Yearbook* appears, one realises that some people must like their anaesthetic literature condensed into short summaries. The experimental design, methods and processing of the results of studies cannot be assessed, so the reader is totally dependent on the editors' critical evaluation and taste. The standard of articles selected, the quality of summaries and the breadth of the field of anaesthesia covered in the 1986 edition are all excellent. The editors' comments are entertaining and thought-provoking. Nevertheless, this reviewer finds that the yearbook is not his method of choice to assimilate the anaesthetic literature and prefers to make his own judgments rather than have those of experts, however distinguished.

The book is divided into 16 sections taken from 70 journals. An initial section called 'The informed anesthesiologist' dwells, *inter alia*, on the value of various pre-operative investigations, the ethical problems of resuscitation and the control (in hospital) of narcotics. The problem of narcotic abuse amongst anaesthesiologists has been stressed in previous yearbooks and continues to be emphasised as a major problem in the United States of America.

The pharmacology section is disappointing because of selection of papers dealing with areas that, in the United Kingdom, would be regarded as yesterday's problems. The effects of etomidate, thiopentone pharmacokinetics and comparisons of narcotics and muscle relaxants seem to present no new data. No paper mentions propofol. Local analgesia techniques are discussed in several articles. It is instructive to be reminded that spinal analgesia failure rates can be as high as 17% in a reputable centre. The main causes were incorrect placement of the drug and inadequate duration of the block.

Critical care medicine is covered extensively. It is interesting to find that hypertonic saline has been rediscovered for the treatment of haemorrhagic shock.

The book would be improved if reviews on apparatus and equipment were included, since devices such as pulse oximeters have swept the market before their calibration and performance have been tested properly. The 1986 *Yearbook* is lively and merits a continued place in the departmental library. It also has an entry for misprint of the year—'Care was also taken to avoid head loss.'

R. GREENBAUM

Advances in Anesthesia, Vol. 4

Edited by R.K. STOELTING, P.G. BARASH AND T.J. GALLAGHER. Pp. 379. Year Book Medical Publishers, Inc., 1987. £38.50.

Volume 4 is the latest in the popular series of collected monographs on a wide variety of topics by American authors. In this volume there are articles on paediatric surgical emergencies, anaesthesia outside the operating room (including the formidable problems of anaesthesia for extracorporeal shock-wave lithotripsy) and the newer investigative procedures such as magnetic resonance imaging. These chapters are essentially practical guides, written in a didactic style, and in each case the author expresses his own preferences freely. A scholarly article on the protection of the brain from hypoxia (with more than 100 references) provides a detailed review of this difficult subject. The chapter on the principles and practice of closed system anaesthesia is as comprehensive as one would expect from one of the leading experts in this field. Chapters on non-invasive monitoring (with a disappointingly brief section on the pulse oximeter), air embolism and the management of patients with hypothyroidism follow. One of the best monographs is that on transfusion therapy. This should be read by all British anaesthetists since it covers the problems and the consequences of advances such as autologous blood transfusion which are currently widely discussed, if not implemented, in the United Kingdom. The book is completed by chapters on antidysrhythmic drugs, prediction of respiratory failure, a review of the pharmacology of the adult respiratory distress syndrome, and the management of acute pain.

There is much to commend in this book. The chapters are plentifully provided with up-to-date references as recent as 1986. Nevertheless, perhaps influenced by the British series of nearly the same name, one can be misled into thinking that the book is *devoted* to *recent* advances. It is not; although it is reassuring to find that the 'traditional' anaesthetic for appendicectomy using thiopentone, suxamethonium, volatile agent, and vecuronium or atracurium is endorsed by the experts, standard practice and new ideas are freely intermingled. There is nothing wrong with this, but the result is a compendium which is neither recent review nor standard textbook. With this proviso, the book (or is it a periodical?) can be recommended to all anaesthetists who look for comprehensive reviews of a range of selected topics.

J.N. HORTON

Companion to the FFARCS Part III

By C. F. CORKE AND I.J.B. JACKSON. Pp. 182. Blackwell Scientific Publications, 1987.

This book is divided into four sections, the largest of which is a series of nearly 100 'Answer plans', each of which consists of brief headings and notes that relate to a particular topic. The purpose of these is two-fold: to provide an aid to revision and to act as a skeleton around which an examination essay can be built. This is followed by a practical clinical section which covers ECGs, chest X rays, pulmonary function tests and blood gas analysis. Ten specimen sets of viva questions and a short section that details some 30 core references (papers of major clinical or historical interest), complete the book.

The answer plans are wide ranging; they cover aspects of anaesthesia for a large variety of patients and conditions, the anatomy of relevant parts of the body and popular examination subjects such as malignant hyperpyrexia and difficult intubation. Most topics are laid out in a logical sequence and particular care is taken to indicate which aspects of management may be regarded by examiners as controversial. Inevitably, in a book of this size, there are many gaps. Regional analgesia has been deliberately omitted by the authors, but there are also no references to obstetric or ophthalmic anaesthesia, halothane hepatitis, closed-system anaesthesia, parenteral nutrition or chronic pain relief, to name but a few. An important section of the new Part III examination is clinical measurement and this has been completely omitted, an odd decision in a book that purports to cover the new syllabus. Indeed, checking five randomly chosen Part III essay papers revealed that only 40% of the questions were usefully covered by this book.

The section of clinical topics is well thought out and the coverage of chest X rays is particularly comprehensive; the descriptions of the radiological appearance of various conditions are so full that the accompanying line diagrams are often superfluous. The viva questions have a ring of authenticity about them, and would be of particular use to tutors preparing mock vivas for their students.

The authors stress that their book should not be regarded as a substitute for the major anaesthetic texts and should be used only as a basis for revision. It may prove a tempting aid to the hard-pressed final fellowship candidate, but its incomplete coverage of the syllabus would make it a dangerous volume on which to rely.

D.G. BOGOD

Anaesthesia, 1987, Volume 42, pages 1136–1146

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for June 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Carcinoid tumours of the rectum and anus. BURKE, M., SHEPHERD, N., MANN, C.V. *British Journal of Surgery* 1987; **74:** 358.

Repeated laparotomy for postoperative intra-abdominal sepsis: an analysis of outcome predictors. BUTLER, J.A., HUANG, J. *et al. Archives of Surgery* 1987; **122:** 702.

Prevention of intraoperative hypothermia during abdominal surgery. JOACHIMSSON, P.O., HEDSTRAND, U. *et al. Acta Anaesthesiologica Scandinavica* 1987; **31:** 330.

Pharmacology

Adrenergic drugs and their antagonists

Clinical pharmacological studies with the long-acting beta-adrenoceptor blocking drug Bopindolol. AELLIG, W.H. *Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 6): S12.

Adimolol, a long acting beta-adrenoceptor blocker in man. ELLION, H.L., JONES, C.R. *et al. British Journal of Clinical Pharmacology* 1987; **23:** 511.

Clinical significance of beta selectivity and intrinsic sympathomimetic activity in a beta-adrenergic blocking drug. FRISHMAN, W.H. *American Journal of Cardiology* 1987; **59:** 26F.

High beta 1-selectivity and favourable pharmacokinetics as the outstanding properties of Bisoprolol. HAEUSLER, G., SCHLIEP, H.J. *et al. Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 11): S2.

Catecholamines predict outcome in traumatic brain injury. HAMILL, R.W., WOOLF, P.D. *et al. Annals of Neurology* 1987; **21:** 438.

Mechanism of inverse regulation of alpha and beta adrenergic receptors. KUMPS, G., ISHAC, E.J.N. *Biochemical Pharmacology* 1987; **36:** 1185.

Hemodynamic effects of dopamine during thoracic epidural analgesia in man. LUNDBERG, J., NORGREN, L. *et al. Anesthesiology* 1987; **66:** 641.

Pharmacological characteristics of beta blockers and their role in clinical practice. MCDEVITT, D.G. *Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 6): S5.

Pharmacologic aspects of intrinsic sympathomimetic activity in beta-blocking drugs. PRICHARD, B.N.C. *American Journal of Cardiology* 1987; **59:** 13F.

Molecular and functional properties of beta-adrenergic receptors. STROSBERG, A.D. *American Journal of Cardiology* 1987; **59:** 3F.

Effect of beta blockers on vascular resistance in systemic hypertension. TVELD, A.J.M.I. *American Journal of Cardiology* 1987; **59:** 21F.

Human liver and conjugation of catecholamines. TYCE, G.M., VAN DYKE, R.A. *et al. Journal of Laboratory and Clinical Medicine* 1987; **109:** 532.

Beta-blockade and carbohydrate metabolism: theoretical aspects and clinical implications. VERSCHOOR, L., WOLFFENBUTTEL, B.H.R., WEBER, R.F. *Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 11): S92.

Anaesthetic agents

Effects of peripheral and central administration of calcium channel blockers in the naloxone-precipitated abstinence syndrome in morphine-dependent rats. BAEYENS, J.M., ESPOSITO, E. *et al. European Journal of Pharmacology* 1987; **137:** 9.

Positron emission tomography assessment of effects of benzodiazepines on regional glucose metabolic rate in patients with anxiety disorder. BUCHSBAUM, M.S., WU, J. *et al. Life Sciences* 1987; **40:** 2393.

A hypothetical model of the mechanism of anesthesia. CHENG, S.C., BRUNNER, E.A. *Medical Hypotheses* 1987; **23:** 1.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Plasma protein extravasation induced by mammalian tachykinins in rat skin: influence of anaesthetic agents and an acetylcholine antagonist. Couture, R., Kerouac, R. *British Journal of Pharmacology* 1987; **91:** 265.

Endocrinological changes following etomidate, midazolam, or methohexital for minor surgery. Crozier, T.A., Beck, D. *et al. Anesthesiology* 1987; **66:** 628.

Acute hepatic damage in rats impairs methorbital metabolism. Farag, M.M., Volicer, L. *Pharmacology* 1987; **34:** 181.

The effect of propofol on adrenocortical steroidogenesis: a comparative study with etomidate and thiopental. Fragen, R.J., Weiss, H.W., Molteni, A. *Anesthesiology* 1987; **66:** 839.

Halothane anesthesia does not suppress sympathetic activation produced by neuroglucopenia. Havel, P.J., Flatness, D.E. *et al. American Journal of Physiology* 1987; **252** (Part I): E667.

Benzodiazepines—structure–activity relationships between D1 receptor blockade and selected pharmacological effects. Lorio, L.C., Barnett, A. *et al.* In: Breese, G.R., Creese, I., eds. *Neurobiology of central D1–dopamine receptors.* New York: Plenum, 1986; p. 1.

Myocardial circulatory and metabolic effects of isoflurane and sufentanil during coronary artery surgery. O'Young, J., Mastrocostostopoulos, G. *et al. Anesthesiology* 1987; **66:** 653.

Isoflurane as an anaesthetic for experimental animal surgery. Raper, S.E., Barker, M.E. *et al. Anatomical Record* 1987; **218:** 116.

Failure of critically ill patients to metabolise midazolam. Shelly, M.P., Mendel, L., Park, G.R. *Anaesthesia* 1987; **42:** 619.

Isoflurane and postoperative hepatic dysfunction. Stoelting, R.K. *Canadian Journal of Anaesthesia* 1987; **34:** 223.

Dextrorphan: an antagonist for phencyclidine receptors. Sun, F.Y., Zhu, H. *et al. Life Sciences* 1987; **40:** 2303.

Analgesic agents

Which potent opioid? Important criteria for selection. Bovill, J.G. *Drugs* 1987; **33:** 520.

Anaesthetic premedication: aims, assessment and methods. Madej, T.H., Paasuke, R.T. *Canadian Journal of Anaesthesia* 1987; **34:** 259.

Comparison of continuous sufentanil and fentanyl infusions for outpatient anaesthesia. Phitayakorn, P., Melnick, B.M., Vicinie, A.F., III. *Canadian Journal of Anaesthesia* 1987; **34:** 242.

Naloxone increases the response of growth hormone and prolactin in stimuli in obese humans. Plewe, G., Schneider, U. *et al. Journal of Endocrinological Investigation* 1987; **10:** 137.

Nonopiate effect of naloxone on cardiac muscle contractility. Sagy, M., Shavit, G. *et al. Journal of Cardiovascular Pharmacology* 1987; **9:** 682.

Effects of morphine and met-enkephalin analogue on gastric lesions induced by indomethacin. Spadaro, C., Arrigo-Reina, R., Scoto, G.M. *Pharmacological Research Communications* 1987; **19:** 223.

Muscle relaxants

Acute and sub-acute inhalation of an organophosphate induce alteration of cholinergic muscarinic receptors. Aas, P., Veiteberg, T.A., Fonnum, F. *Biochemical Pharmacology* 1987; **36:** 1261.

Prevention of physostigmine-induced lethality by the opioid analgesic meptazinol in the mouse. Bottoncetti, A., Galli, A. *British Journal of Pharmacology* 1987; **91:** 299.

Unequal effects of cardiopulmonary bypass-induced hypothermia on neuromuscular blockade from constant infusion of alcuronium, d-tubocurarine, pancuronium. Buzello, W., Schluermann, D. *et al. Anesthesiology* 1987; **66:** 842.

Aggressive surgical approach for drug-free remission from myasthenia gravis. Fischer, J.E., Grinvalski, H.T. *et al. Annals of Surgery* 1987; **205:** 496.

Concentration-dependent interaction of theophylline with d-tubocurarine. Fuke, N., Martyn, J. *et al. Journal of Applied Physiology* 1987; **62:** 1970.

Respiratory failure in Lambert–Eaton myasthenic syndrome. Gracey, D.R., Southorn, P.A. *Chest* 1987; **91:** 716.

Acetylcholine-receptor-like protein from human thymoma associated with myasthenia gravis. Kawanami, S., Kamei, H. *et al. Journal of Neurology* 1987; **234:** 207.

Inhibition of d-turbocurarine-induced histamine release by halothane. Kettlekamp, N.S., Austin, D.R. *et al. Anesthesiology* 1987; **66:** 666.

Aminoglycosides and 3,4-diaminopyridine on neuromuscular block caused by botulinum type A toxin. Molgo, J., Lemeignan, M., Thesleff, S. *Muscle and Nerve* 1987; **10:** 464.

Anticholinergic pharmacological studies of the lower oesophageal sphincter: importance of the technique of pressure recording. Ndjitoyap, C., Lerebours, E. *et al. International Journal of Clinical Pharmacology Research* 1987; **7:** 89.

'A' esterases and their role in regulating the toxicity of organophosphates. Walker, C.H., MacKness, M.I. *Archives of Toxicology* 1987; **60:** 30.

Effects of (+)-tubocurarine on [3H]acetylcholine release from the rat phrenic nerve at different stimulation frequencies and train lengths. Wessler, I., Rasbach, J. *et al. Archives of Pharmacology* 1987; **335:** 496.

Other drugs

Steady-state pharmacokinetics of metronidazole in

Crohn's disease. Eradiri, O., Jamali, F., Thompson, A.B.R. *Biopharmaceutics and Drug Disposition* 1987; **8:** 249.

Anesthetic mishaps: breaking the chain of accident evolution. Gaba, D.M., Maxwell, M., Deanda, A. *Anesthesiology* 1987; **66:** 670.

Early adventures in drug metabolism. 2. The absorption of drugs. Glazko, A.J. *Therapeutic Drug Monitoring* 1987; **9:** 180.

Conjugation–deconjugation reactions in drug metabolism and toxicity. Kauffman, F.C. *Federation Proceedings* 1987; **45:** 2434.

Therapeutic aminoglycoside monitoring in renal failure patients. Keller, F., Borner, K. *et al. Therapeutic Drug Monitoring* 1987; **9:** 148.

Drug interactions in surgical patients. May, J.R., Dipiro, J.T., Sisley, J.F. *American Journal of Surgery* 1987; **153:** 327.

Reduction of metformin renal tubular secretion of cimetidine in man. Somogyi, A., Stockley, C. *et al. British Journal of Clinical Pharmacology* 1987; **23:** 545.

Basic concepts in drug metabolism. Woolf, T.J., Jordan, R.A. *Journal of Clinical Pharmacology* 1987; **27:** 15.

Apparatus

Electrical safety in the operating room. Buczko, G.B., McKay, W.P.S. *Canadian Journal of Anaesthesia* 1987; **34:** 315.

Measurements of hemoglobin oxygen saturation in capillaries. Ellsworth, M.L., Pittman, R.N., Ellis, C.G. *American Journal of Physiology* 1987; **252** (Part 2): H1031.

Safe jugular and subclavian venipuncture under ultrasonographic guidance. Machi, J., Takeda, J., Kakegawa, T. *American Journal of Surgery* 1987; **153:** 321.

Methodological problems related to measurement of quantitative blood flow with the ultrasound Doppler technique. Rasmussen, K. *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **17:** 303.

A phrenic nerve-actuated electronically controlled positive-pressure ventilator. Schertel, E.R., Schneider, D.A. *et al. Journal of Applied Physiology* 1987; **62:** 2121.

Complications

Postoperative complications due to paradoxical vocal cord motion. Hammer, G., Schwinn, D., Wallmann, H. *Anesthesiology* 1987; **66:** 686.

C5a and thromboxane generation associated with pulmonary vaso- and bronchoconstriction during protamine reversal of heparin. Morel, D.R., Zapol, W.M. *et al. Anesthesiology* 1987; **66:** 597.

Unusual neurotoxicity associated with amiodarone therapy. Palakurthy, P.R., Iyer, V., Meckler, R.J. *Archives of Internal Medicine* 1987; **147:** 881.

General anaesthetic procedures

Retention of auditory information presented during anaesthesia. A study of children who received light general anaesthesia. Standen, P.J., Hain, W.R., Hosker, K.J. *Anaesthesia* 1987; **42:** 604.

Intraoperative respiratory complications in patients with upper respiratory tract infections. Tait, A.R., Knight, P.R. *Canadian Journal of Anaesthesia* 1987; **34:** 300.

General interest

Amnesia–organic and psychogenic. Kopelman, M.D. *British Journal of Psychiatry* 1987; **150:** 428.

Clinical spectrum of hereditary hemorrhagic telangiectasis. Peery, W.H. *American Journal of Medicine* 1987; **82:** 989.

Reflex sympathetic dystrophy: a review. Schwartzman, R.J., McLellan, T.L. *Archives of Neurology* 1987; **44:** 555.

Local analgesia

The effect of lipid composition on the metabolism of lignocaine by a reconstituted mixed function oxidase system from rat liver. Meftah, N.M., Skett, P. *Biochemical Pharmacology* 1987; **36:** 1203.

Postoperative pain relief and bupivacaine plasma levels during continuous interscalene brachial plexus block. Tuominen, M., Pikanen, M., Rosenberg, P.H. *Acta Anaesthesiologica Scandinavica* 1987; **31:** 276.

Effects of procaine on pharmaco–mechanical coupling mechanisms activated by acetylcholine in smooth muscle cells of porcine coronary artery. Ueno, H., Sumimoto, K. *et al. Circulation Research* 1987; **60:** 356.

Spinal and epidural analgesia

Neurotoxicology of spinal agents. Coombs, D.W., Fratkin, J.D. *Anesthesiology* 1987; **66:** 724.

Hypotension in spinal anaesthesia: a comparison of isobaric tetracaine with epinephrine and isobaric bupivacaine without epinephrine. Phero, J.C., Bridenbaugh, P.O. *et al. Anesthesia and Analgesia* 1987; **66:** 549.

Epidural steroid injection as a predictor of surgical outcome. Warfield, C.A. Crews, D.A. *Surgery, Gynecology and Obstetrics* 1987; **164:** 457.

Epidural anesthesia and analgesia in high-risk surgical patients. Yeager, M.P., Glass, D.D. *et al. Anesthesiology* 1987; **66:** 729.

Spinal opioids

Label for the opioid receptor. Benyhe, S., Hepp, J. *et al. Neuropeptides* 1987; **9:** 237.

Opioid control of oxytocin secretion: evidence of distinct regulatory actions of two opiate receptor types. Carter, D.A., Lightman, S.L. *Life Sciences* 1987; **40:** 2289.

The role of enkephalins in the production of epileptogenic activity and autonomic dysfunction: origin of arrhythmia and sudden death in epileptic patients? Kraras, C.M., Tumer, N., Lathers, C.M. *Medical Hypotheses* 1987; **23:** 19.

Role of mu and delta receptors in the supraspinal and spinal analgesic effects of [D-Pen2, D-Pen5]. Porreca, F., Heyman, J.S. *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; **241:** 393.

Obstetric anaesthesia and analgesia

The influence of continuous epidural bupivacaine analgesia on the second stage of labor and method of delivery in nulliparous women. Chestnut, D.H., Vanderwalker, G.E. *et al. Anesthesiology* 1987; **66:** 774.

Oxytocin and vasopressin: distinct receptors in myometrium. Guillon, G., Balestre, M.N. *et al. Journal of Clinical Endocrinology and Metabolism* 1987; **64:** 1129.

A comparative study of transcutaneous electrical nerve stimulation (TENS), entonox, pethidine + promazine and lumbar epidural for pain relief in labour. Harrison, R.F., Shore, M. *et al. Acta Obstetrica et Gynecologica Scandinavica* 1987; **66:** 9.

Myasthenic crisis in the puerperium: the possible importance of alpha-fetoprotein. Case report. Hatada, Y., Munemura, M. *et al. British Journal of Obstetrics and Gynaecology* 1987; **94:** 480.

Maternal obesity and pregnancy. Johnson, S.R., Kolberg, B.H. *et al. Surgery, Gynecology and Obstetrics* 1987; **164:** 431.

The effect of epidural analgesia on the frequency of instrumental obstetric delivery. Kaminski, H.M., Staft, A., Aiman, J. *Obstetrics and Gynecology* 1987; **69:** 770.

The effect of the duration of the second stage of labour on the acid–base state of the fetus. Katz, M., Lunenfeld, E. *et al. British Journal of Obstetrics and Gynaecology* 1987; **94:** 425.

Continuous extradural analgesia: catch-up or top-up? Leading article. *Lancet* 1987; **1:** 1300.

Arterial blood pressure standards during normal pregnancy and their relation with mother fetus variables. Margulies, M., Voto, L.S. *et al. American Journal of Obstetrics and Gynecology* 1987; **156:** 1105.

Serial noninvasive evaluation of cardiovascular hemodynamics during pregnancy. Mashini, I.S., Albazzaz, S.J. *et al. American Journal of Obstetrics and Gynecology* 1987; **156:** 1208.

Noninvasive measurement of gastric emptying in obstetric patients. O'Sullivan, G.M., Sutton, A.J. *et al. Anesthesia and Analgesia* 1987; **66:** 505.

Obstetrical anaesthesia at Winnipeg Women's Hospital 1975–1983. Anaesthetic techniques and complications. Ong, B., Cohen, M.M. *et al. Canadian Journal of Anaesthesia* 1987; **34:** 294.

Pulmonary edema in severe preeclampsia–eclampsia. Analysis of 37 consecutive cases. Sibai, B.M., Mabie, B.C. *et al. American Journal of Obstetrics and Gynecology* 1987; **156:** 1174.

The feasibility of closed mitral valvotomy and pregnancy. Vasloo, S., Reichart, B. *Journal of Thoracic and Cardiovascular Surgery* 1987; **93:** 675.

Paediatric anaesthesia and intensive care

Effect of antepartum ritodrine on the cardiorespiratory status of the newborn after elective cesarean section. Aarimaa, T., Ekblad, U. *et al. Gynecologic and Obstetric Investigation* 1987; **23:** 160.

Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. Bancalari, E., Flynn, J. *et al. Pediatrics* 1987; **79:** 663.

Cytochrome P-450 in the mitochondria from human placenta in early pregnancy. Boguslawski, W. *Biological Research in Pregnancy and Perinatology* 1987; **8:** 16.

Prolonged mechanical ventilation and intracranial pressure hemorrhage—impact on progress in infants weighing 1,200 grams. Bozynski, M.E.A., Nelson, M.N. *et al. Pediatrics* 1987; **79:** 670.

Cardiac performance in children with homozygous sickle cell disease. Chung, E.E., Dianzumba, S.B. *et al. Journal of the American College of Cardiology* 1987; **9:** 1038.

Indomethacin does not alter the circulation catecholamine response to asphyxia in the neonatal piglet. Green, R.S., Leffer, C.W. *et al. Pediatric Research* 1987; **21:** 534.

Expiratory volume clamping: a new method to assess respiratory mechanics in sedated infants. Grunstein, M.M., Springer, C. *et al. Journal of Applied Physiology* 1987; **62:** 2107.

Haemoglobin O_2 binding in newborn and adult rabbits. Holter, P.H., Kieruf, P., Refsum, H.E. *Acta Physiologica Scandinavica* 1987; **130:** 349.

Control of human placental blood flow. Howard, R.B. *Medical Hypotheses* 1987; **23:** 51.

Fatal outcome of methemoglobinemia in an infant. Johnson, C.J., Bonnud, P.A. *et al. Journal of the American Medical Association* 1987; **257:** 2796.

The effect of segmental epidural analgesia on the neurobehavioural responses of newborn infants. Kangassaarela, T., Jouppila, R. *et al. Acta Anaesthesiologica Scandinavica* 1987; **31:** 347.

Vasopressin functions as an endogenous antipyretic in the newborn. KASTING, N.W., WILKINSON, M.F. *Biology of the Neonate* 1987; **51:** 249.

Pulmonary lesions of thalassemia major. LANDING, B.H., NADORRA, R. *et al.* In: ROSENBERG, H.S., BERNSTEIN, J., eds. *Respiratory and alimentary tract diseases*. Basel: Karger AG, 1987; p. 82.

Carbon dioxide tensions in infants during mask anaesthesia with spontaneous ventilation. LARSSON, L.E., ANDREASSON, S. *et al. Acta Anaesthesiologica Scandinavica* 1987; **31:** 273.

Postoperative hypertension after repair of coarctation of aorta in children: protective effect of propranolol? LEENEN, F.H.H., BALFE, J.A. *et al. American Heart Journal* 1987; **113:** 1164.

Transcutaneous oxygen measurement in paediatric respiratory disease. LOFTUS, B.G., BARRY, W., PRICE, J.F. *British Journal of Diseases of the Chest* 1987; **81:** 128.

Effect of the energy source on changes in energy expenditure, respiratory quotient and nitrogen balance during total parenteral nutrition in children. NOSE, O., TIPTON, J.R. *et al. Pediatric Research* 1987; **21:** 538.

The association between cardiovascular response tasks and future blood pressure levels in children: Bogalusa heart study. PARKER, F.C., CROFT, J.B. *et al. American Heart Journal* 1987; **113:** 1174.

Pathology of neonatal surfactant deficiency. ROBERTSON, B. In: ROSENBERG, H.S., BERNSTEIN, J., eds. *Respiratory and alimentary tract diseases*. Basel: Karger AG, 1987; p. 6.

Infantile apnoea and home monitoring. SIMPSON, H. *British Medical Journal* 1987; **294:** 1367.

Cerebral metabolic response of hyperglycemic immature rats to hypoxia–ischemia. VANNUCCI, R.C., VASTA, F., VANNUCCI, S.J. *Pediatric Research* 1987; **21:** 524.

Prolongation of inspiration during lower airway occlusion in children. WITTE, M.K., CARLO, W.A. *Journal of Applied Physiology* 1987; **62:** 1860.

Ventilatory management of infant baboons with hyaline membrane disease: the use of high frequency ventilation. DELEMOS, R.A., COALSON, J.J. *et al. Pediatric Research* 1987; **21:** 594.

Cardiovascular system

Physiology

Myocardial contractile function during ischemia and hypoxia. ALLEN, D.G., ORCHARD, C.H. *Circulation Research* 1987; **60:** 153.

The fundamental hemodynamic mechanism underlying gastric 'stress ulceration' in cardiogenic shock. BAILEY, R.W., BULKLEY, G.B. *et al. Annals of Surgery* 1987; **205:** 597.

Nonadrenergic neural vasodilator mechanisms. BEVAN, J.A., BRAYDEN, J.E. *Circulation Research* 1987; **60:** 309.

Cardiac and vascular beta-adrenoceptor-mediated responses before and during treatment with Bisoprolol or Atenolol. BOLLI, P., MULLER, F.B. *et al. Journal of Cardiovascular Pharmacology* 1986: **8** (Suppl. 11): S61.

Reversible and irreversible nodal dysfunction in diabetic neuropathy. BRISMAR, T., SIMA, A.A.F., GREENE, D.A. *Annals of Neurology* 1987; **21:** 504.

Renal mechanisms of human alpha-atrial natriuretic peptide in man. BROWN, J., CORR, L. *Journal of Physiology* 1987; **387:** 31.

Quantitative in vitro autoradiographic localization of angiotensin II receptor binding and angiotensin converting enzyme in target tissues. CHAI, S.Y., ALLEN, A.M. *et al. Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 10): S35.

Neuroendocrine activation in acute myocardial infarction. DARGIE, H.J., MCALPINE, H.M., MORTON, J.J. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 2): S21.

Preload dependence of right ventricular blood flow. 1. The normal right ventricle. DYKE, C.M., LOUIS, A.B. *et al. Annals of Thoracic Surgery* 1987; **43:** 478.

Human atrial natriuretic peptide. ESPINER, E.A., NICHOLLS, M.G. *Clinical Endocrinology* 1987; **26:** 637.

Neurogenic hypertension associated with an excessively high excretion rate of catecholamine metabolites. FUNCK-BRENTANO, C., PAGNY, J.Y., MENARD, J. *British Heart Journal* 1987; **57:** 487.

Relation of arterial blood lactate to oxygen delivery and hemodynamic variables in human shock states. GROENEVELD, A.B.J., KESTER, A.D.M. *et al. Circulatory Shock* 1987; **22:** 35.

Central nervous system is involved in the cardiovascular responses to naloxone in canine endotoxic but not hemorrhagic shock. GURLL, N.J., GANES, E., REYNOLDS, D.G. *Circulatory Shock* 1987; **22:** 115.

Renal excretory function and hypertension. HALL, J.E., GUYTON, A.C. *et al.* In: KAPLAN, N.M. *et al.*, eds. *Kidney in hypertension*. New York: Raven Press, 1987; p. 1.

Hemodynamic changes and renal plasma flow in early heart failure: implications for renin, aldosterone, norepinephrine, ANP and prostacyclin. HOLMER, S.R., RIEGGER, A.J.G. *et al. Basic Research in Cardiology* 1987; **82:** 101.

Increased capillary hydraulic conductivity induced by atrial natriuretic peptide. HUXLEY, V.H., TUCKER, V.L. *et al. Circulation Research* 1987; **60:** 304.

Arrhythmias and sudden death in mitral valve prolapse. KLIGFIELD, P., LEVY, D. *et al. American Heart Journal* 1987; **113:** 1298.

Plasma atrial natriuretic factor concentrations in essential and renovascular hypertension. LAROCHELLE, P., CUSSON, J.R. *et al. British Medical Journal* 1987; **294:** 1249.

Prevalence and clinical features of mitral valve prolapse. Levy, D., Savage, D. *American Heart Journal* 1987; **113:** 1281.

Humoral factors in primate endotoxin shock. May, M., Pohlson, E.C. *et al. Circulatory Shock* 1987; **22:** 127.

The role of calcium in ischemic myocardial injury. Murphy, J.G., Marsh, J.D., Smith, W.T. *Circulation* 1987; **75** (Part 6, Suppl.): V15.

The clinical significance of intrinsic sympathomimetic activity. Northcote, R.J. *International Journal of Cardiology* 1987; **15:** 133.

Actions of calcium antagonists on pre- and post-junctional effects of neuropeptide Y on human peripheral blood vessels *in vitro*. Pernow, J., Svenberg, T., Lundberg, J.M. *European Journal of Pharmacology* 1987; **136:** 207.

Ventricular enlargement following a myocardial infarction. Pfeffer, M.A., Pfeffer, J.M. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 2): S18.

Hemodynamic response to fluid repletion in patients with septic shock: evidence for early depression of cardiac performance. Rackow, E.C., Kaufman, B.S. *et al. Circulatory Shock* 1987; **22:** 11.

Lung and cardiac reflex actions on the tracheal vasculature in anaesthetized dogs. Sahin, G., Webber, S.E., Widdicombe, J.G. *Journal of Physiology* 1987; **387:** 47.

Ion transport in circulatory and/or septic shock. Sayeed, M.M. *American Journal of Physiology* 1987; **252** (Part 2): R809.

Takayasu's arteritis and myocardial dysfunction. Schamroth, C.L., Sareli, P. *et al. American Heart Journal* 1987; **113:** 1240.

Plasma zinc and myocardial infarction: new hypothesis. Speich, M. *Journal of the American College of Nutrition* 1987; **6:** 187.

Absence of progression of left ventricular hypertrophy in adult patients with hypertrophic cardiomyopathy. Spirito, P., Maron, B.J. *Journal of the American College of Cardiology* 1987; **9:** 1013.

Effects of oral labetalol on forearm and hepatic circulations in normotensive humans. Sweeney, M.O., Cinquegrank, M., Liang, C.-S. *Journal of Laboratory and Clinical Medicine* 1987; **109:** 589.

The effects of calcium-entry blockade on left ventricular systolic and diastolic function. Walsh, R.A. *Circulation* 1987; **75** (Part 5, Suppl.): V43.

Contrasting patterns of autonomic dysfunction in patients with mitral valve prolapse and panic attacks. Weissman, N.J., Shear, M.K. *et al. American Journal of Medicine* 1987; **82:** 880.

Beta-adrenergic regulation of cardiac myosin. Winegrad, S., McClellan, G. *et al. Canadian Journal of Physiology and Pharmacology* 1987; **65:** 606.

Cerebral ischemia with mitral valve prolapse. Wolf, P.A., Sila, C.A. *American Heart Journal* 1987; **113:** 1308.

Treatment and medication

Prevention of deep venous thrombosis in patients with acute spinal cord injuries: use of rotating treatment tables. Becker, D.M., Gonzalez, M. *et al. Neurosurgery* 1987; **20:** 675.

Esmolol: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. Benfield, P., Sorkin, E.M. *Drugs* 1987; **33:** 392.

Clinical types of proarrhythmic response to antiarrhythmic drugs. Bigger, J.T., Jr, Sahar, D.I. *American Journal of Cardiology* 1987; **59:** 2E.

Recent advances in the identification of patients at risk of ventricular tachyarrhythmia: role of ventricular late potentials. Breithardt, G., Borggrefe, M. *Circulation* 1987; **75:** 1091.

Hazards of intravenous verapamil for sustained ventricular tachycardia. Buxton, A.E., Marchlinski, F.E. *et al. American Journal of Cardiology* 1987; **59:** 1107.

The cardioselective and hypotensive effects of Bisoprolol in hypertensive asthmatics. Chatterjee, S.S. *Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 11): S74.

Clinical, haemodynamic, and antiarrhythmic effects of long term treatment with amiodarone of patients in heart failure. Cleland, J.G.F., Dargie, H.J. *et al. British Heart Journal* 1987; **57:** 436.

Buflomedil: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in peripheral and cerebral vascular diseases. Clissold, S.P., Lynch, S., Sorkin, E.M. *Drugs* 1987; **33:** 430.

Intra-arterial vasodilator agents to reverse human finger vasoconstriction. Coffman, J.D., Cohen, R.A. *Clinical Pharmacology and Therapeutics* 1987; **41:** 574.

Arterial reactivity, BP and plasma levels of ANP in normotensive and hypertensive rats: effects of acute and chronic administration of atriopeptin III. De Mey, J.G., Defreyn, G. *et al. Journal of Cardiovascular Pharmacology* 1987; **9:** 525.

Effects of vasodilator antihypertensive agents on renal function. DiBona, G.F. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 1): S14.

Induced hypotension: action of sodium nitroprusside and nitroglycerin on the microcirculation: a micropuncture investigation. Endrich, B., Franke, N. *et al. Anesthesiology* 1987; **66:** 605.

A review of medical therapy for coronary artery spasm. Feldman, R.L. *Circulation* 1987; **75** (Part 6, Suppl.): V96.

Drug therapy: dipyridamole. Fitzgerald, G.A. *New England Journal of Medicine* 1987; **316:** 1247.

The relative contributions of antithrombin III during heparin treatment and of risk factors, to early recurrence of venous thromboembolism. Gallus, A.S., Goodall, K.T. *et al. Thrombosis Research* 1987; **46:** 539.

Functional properties of hemoglobin in human red cells. I. Oxygen equilibrium curves and DPG binding. GIRARD, F., KISTER, J. *et al. Respiration Physiology* 1987; **68:** 227.

Low molecular weight heparin fractions as an alternative therapy in heparin-induced thrombocytopenia. GOUAULT-HEILMANN, M., HUET, Y. *et al. Haemostasis* 1987; **17:** 134.

Routine use of beta-blockers following myocardial infarction: a note of dissent. GREENBAUM, R.A. *Journal of the Royal Society of Medicine* 1987; **80:** 402.

Experience with nalbuphine, a new opioid analgesic, in acute myocardial infarction. GREENBAUM, R.A., KAYE, G., MASON, P.D. *Journal of the Royal Society of Medicine* 1987; **80:** 418.

Heparin resistance induced by intravenous nitroglycerin—a word of caution when both drugs are used concomitantly. HABBAB, M.A., HAFT, J.I. *Archives of Internal Medicine* 1987; **147:** 857.

Effect of autonomic blockade on the hemodynamic responses of normal human subjects to acute intravenous milrinone. HASKINT, T.J., DEWAR, E. *et al. Journal of Cardiovascular Pharmacology* 1987; **9:** 515.

Spontaneous conversion of ventricular fibrillation in cardiogenic shock from acute myocardial infarction. INTERIAN, A., JR, TROHMAN, R.G. *et al. American Journal of Cardiology* 1987; **59:** 1200.

The renal actions of nitrendipine and its influence on the neural regulation of calcium and sodium reabsorption in the rat. JOHNS, E.J., MANITIUS, J. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 1): S49.

Principles of antihypertensive drug therapy—an overview. KAPLAN, N.M. In: KAPLAN, N.M. *et al.*, eds. *Kidney in hypertension*. New York: Raven Press, 1987; p. 127.

Constant postoperative monitoring of cardiac output after correction of congenital heart defects. KEAGY, B.A., WILCOX, B.R. *et al. Journal of Thoracic and Cardiovascular Surgery* 1987; **93:** 658.

Painful sickle cell crises precipitated by stopping prophylactic exchange transfusions. KEIDAN, A.J., MARWAH, S.S. *et al. Journal of Clinical Pathology* 1987; **40:** 505.

Incidence risk, and outcome of reintervention after aortocoronary bypass surgery. LAIRD-MEETER, K., VAN DOMBURG, R. *et al. British Heart Journal* 1987; **57:** 427.

Prevention of myocardial electrical activity during ischemic arrest with verapamil cardioplegia. LANDYMORE, R.W., MARBLE, A.E. *et al. Annals of Thoracic Surgery* 1987; **43:** 534.

Cardiac arrhythmia, sudden death, and psychoactive agents. LATHERS, C.M., LIPKA, L.J. *Journal of Clinical Pharmacology* 1987; **27:** 1.

Vasodilators and regression of left ventricular hypertrophy. Hydralazine versus prazosin in hypertensive humans. LEENEN, F.H.H., SMITH, D.L. *et al. American Journal of Medicine* 1987; **82:** 969.

Value of nutritional parameters in the prediction of postoperative complications in elective gastrointestinal surgery. LEITE, J.F.M., ANTUNES, C.F. *et al. British Journal of Surgery* 1987; **74:** 426.

Suppressor T lymphocyte function in patients with idiopathic congestive cardiomyopathy. LOWRY, P.J., GAMMAGE, M.D. *et al. British Heart Journal* 1987; **57:** 458.

Pathogenesis and management of septic shock. LUCE, J.M. *Chest* 1987; **91:** 883.

Quality of life after coronary artery surgery. MAYOU, R., BRYANT, B. *Quarterly Journal of Medicine* 1987; **62:** 239.

Caffeine as a possible cause of ventricular arrhythmias during the healing phase of acute myocardial infarction. MYERS, M.G., HARRIS, L. *et al. American Journal of Cardiology* 1987; **59:** 1024.

Haemodynamic effects of captorpril in acute left ventricular failure complicating myocardial infarction. MCALPINE, H.M., MORTON, J.J. *et al. Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 2): S25.

Calcium-entry blockade: basic concepts and clinical implications. Introduction. O'ROURKE, R.A. *Circulation* 1987; **75** (Part 2, Suppl.): V1.

Provocative testing with prolonged hyperventilation and ergometrine in patients suspected of coronary artery spasm—a comparative study. RASMUSSEN, K., HENNINGSEN, P. *International Journal of Cardiology* 1987; **15:** 151.

Arrhythmogenic actions of antiarrhythmic drugs. ROSEN, M.R., WIT, A.L. *American Journal of Cardiology* 1987; **59:** 10E.

Red cell age effects on metabolism and oxygen affinity in humans. SCHMIDT, W., BONING, D., BRAUMANN, K.M. *Respiration Physiology* 1987; **68:** 215.

Hemodynamic and neurohumoral response to hydralazine versus captopril: a controlled study in idiopathic dilated cardiomyopathy. SCHOFER, J., MATHEY, D.G. *et al. Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 2): S46.

Long-term intellectual dysfunction following coronary artery bypass graft surgery—a 6-month followup study. SHAW, P.J., BATES, D. *et al. Quarterly Journal of Medicine* 1987; **62:** 259.

Intraoperative myocardial protection in the context of coronary revascularization. SILVERMAN, N.A., LEVITSKY, S. *Progress in Cardiovascular Diseases* 1987; **29:** 413.

Nicardipine: a review of its therapeutic efficacy in the treatment of angina pectoris, hypertension and related cardiovascular disorders. SORKIN, E.M., CLISSOLD, S.P. *Drugs* 1987; **33:** 296.

Postoperative water and electrolyte changes in skeletal muscle—a clinical study with 3 different intravenous infusions. STILLSTORM, A., PERSSON, E. *Acta Anaes-*

thesiologica Scandinavica 1987; **31:** 284.

Comparison of blood and crystalloid cardioplegia during heart transplantation after 5 hours of cold storage. Swanson, D.K., Myerowitz, D. *et al. Journal of Thoracic and Cardiovascular Surgery* 1987; **93:** 687.

Vasodilators and beta-adrenergic antagonists. Textor, S.C. In: Kaplan, N.M. *et al.*, eds. *Kidney in hypertension*. New York: Raven Press, 1987; p. 145.

Beta-blocker therapy and the risk of anaphylaxis. Toogood, J.H. *Canadian Medical Association Journal* 1987; **136:** 929.

A prospective study of thymopentin in severely burned patients. Waymack, J.P., Jenkins, M. *et al. Surgery, Gynecology and Obstetrics* 1987; **164:** 423.

Newer positive inotropic agents in the treatment of chronic cardiac failure: current status and future directions. Weber, K.T., Gill, S.K. *et al. Drugs* 1987; **33:** 503.

Nutritional aspects of preoperative management. Weiss, S.M. *Medical Clinics of North America* 1987; **71:** 369.

Antihypertensive therapy and cardiovascular complications. Zanchetti, A. *Journal of Cardiovascular Pharmacology* 1986; **8** (Suppl. 6): S34.

Respiration

Physiology

Pulmonary function in thyroid carcinoma metastatic to the lung. Aldrich, L.B., Sisson, J.C., Grum, C.M. *Journal of Endocrinological Investigation* 1987; **10:** 111.

Effects of continuous positive airway pressure on upper airway and respiratory muscle activity. Alex, C.G., Aronson, R.M. *et al. Journal of Applied Physiology* 1987; **62:** 2026.

Autonomic control of airway function in asthma. Barnes, P.J. *Chest* 1987; **91** (Suppl.): 45S.

Tracheal pressure and impedance as determinants of gas exchange during high frequency ventilation. Clarke, J.R., Homer, L.D. *et al. Respiration Physiology* 1987; **68:** 121.

Bedside measurement of pulmonary capillary pressure in patients with acute respiratory failure. Collee, G.G., Lynch, K.E. *et al. Anesthesiology* 1987; **66:** 614.

Adaptation to chronic hyperoxia—biochemical effects and the response to subsequent lethal hyperoxia. Coursin, D.B., Cihla, H.P. *et al. American Review of Respiratory Disease* 1987; **135:** 1002.

Effects of intermittent negative pressure ventilation on respiratory muscle function in patients with severe chronic obstructive pulmonary disease. Cropp, A., DiMarco, A.F. *American Review of Respiratory Disease* 1987; **135:** 1056.

Ventilation–perfusion inequality in lung disease. Dantzker, D.R. *Chest* 1987; **91:** 749.

Breathing pattern abnormalities and arterial oxygen desaturation during sleep in the congestive heart failure syndrome. Dark, D.S., Pingleton, S.K. *et al. Chest* 1987; **91:** 833.

Sympathetic innervation of human tracheal and bronchial smooth muscle. Davis, C., Kannan, M.S. *Respiration Physiology* 1987; **68:** 53.

Pharmacodynamic mechanism and therapeutic activity of ambroxol in animal experiments. Disse, B.G., Ziegler, H.W. *Respiration* 1987; **51:** 15.

Prediction of postoperative pulmonary complications in oesophagogastric cancer surgery. Fan, S.T., Lau, W.Y. *et al. British Journal of Surgery* 1987; **74:** 408.

Characteristics of a simple measure of respiratory impedance. Fordyce, W.E., Whetstone, R.M. *Respiration Physiology* 1987; **68:** 145.

Closing volume after inspiratory resistive loading to fatigue. Gallagher, G.G., Younes, M. *Respiration Physiology* 1987; **68:** 137.

The causes and evaluation of chronic hypercapnea. Glauser, F.L., Fairman, R.P., Bechard, D. *Chest* 1987; **91:** 755.

Reversal of sleep-induced hypoventilation and respiratory failure by nocturnal negative pressure ventilation in patients with restrictive ventilation. Goldstein, R.S., Molotiu, N. *et al. American Review of Respiratory Disease* 1987; **135:** 1049.

Mechanisms of oxygen-induced lung injury. Housset, B. *Archives Internationales de Physiologie et de Biochimie* 1987; **94:** S1.

Arterial oxygen saturation and breathlessness in patients with chronic obstructive airways disease. Lane, R., Cockcroft, A. *et al. Clinical Science* 1987; **72:** 693.

Surfactant synthesis, secretion and function in alveoli and small airways. Review of the physiologic basis for pharmacologic intervention. Mason, R.J. *Respiration* 1987; **51:** 3.

Hypoxic pulmonary vasoconstriction and pulmonary gas exchange in normal man. Melot, C., Naeije, R. *et al. Respiration Physiology* 1987; **68:** 11.

Airway hyperreactivity in COPD; cause or effect, in *in vivo*, *in vitro* comparison. Pare, P.D., Armour, C. *et al. Chest* 1987; **91** (Suppl.): 40S.

Plasticity of the mechanism subserving inspiratory load perception. Revelette, W.R., Wiley, R.L. *Journal of Applied Physiology* 1987; **62:** 1901.

Gas exchange and pulmonary vascular reactivity in patients with liver cirrhosis. Rodriguezroisin, R., Roca, J. *et al. American Review of Respiratory Disease* 1987; **135:** 1085.

Asthma and bronchial reactivity. Scadding, J.G. *British Medical Journal* 1987; **294:** 1115.

Tissue oxygen extraction during hypovolemia: role of hemoglobin P50. Schumacker, P.T., Long, G.R., Wood, L.D.H. *Journal of Applied Physiology* 1987; **62:** 1801.

Expiratory activity in transferred intercostal nerves in brachial plexus injury patients. Sibuya, M., Homma, I. *et al. Journal of Applied Physiology* 1987; **62:** 1780.

Failure of ipratropium bromide to modify the diurnal variation of asthma in asthmatic children. Sly, P.D., Landau, L.I., Olinsky, A. *Thorax* 1987; **42:** 353.

Effect of lung volume on *in vivo* contraction characteristics of human diaphragm. Smith, J., Bellemare, F. *Journal of Applied Physiology* 1987; **62:** 1893.

Surfactant and physiologic alterations in an animal model of adult human lung disease. A preliminary report. Sulavik, S.B., Thrall, R.S. *Respiration* 1987; **51:** 10.

Effect of lung volume on breath holding. Whitelaw, W.A., McBride, B., Ford, G.T. *Journal of Applied Physiology* 1987; **62:** 1962.

Geometry and respiratory displacement of human ribs. Wilson, T.A., Rehder, K. *et al. Journal of Applied Physiology* 1987; **62:** 1872.

Treatment and medication

Response to inhaled bronchodilators in COPD. Anthonisen, N.R., Wright, E.C. *Chest* 1987; **91** (Suppl.): 36S.

Mouth intermittent positive pressure ventilation in the management of postpolio respiratory insufficiency. Bach, J.R., Alba, A.S. *et al. Chest* 1987; **91:** 859.

Effect of combined use of intravenous salbutamol and aminophylline on cardiac rhythm in chronic obstructive lung disease. Bigi, R., Camerone, G. *et al. Respiration* 1987; **51:** 119.

Effects of inhaled lidocaine on exercise-induced asthma. Chen, W.Y., Chai, H. *Respiration* 1987; **51:** 91.

Respiratory system mechanics in ventilated patients: techniques and indications. Hubmayr, R.D., Gay, P.C., Tayyab, M. *Mayo Clinic Proceedings* 1987; **62:** 358.

Whole-lung lavage under hyperbaric oxygen condition for alveolar proteinosis with respiratory failure. Jansen, H.M., Zuurmond, W.W.A. *et al. Chest* 1987; **91:** 829.

Predictors of successful weaning in ventilated patients. Leading article. *Lancet* 1987; **1:** 1245.

Aerosol therapy of reversible airflow obstruction: concepts and clinical applications. Newhouse, M.T., Dolovich, M. *Chest* 1987; **91** (Suppl.): 58S.

Nutritional management in acute respiratory failure. Pingleton, S.K., Harmon, G.S. *Journal of the American Medical Association* 1987; **257:** 3094.

Asthma—emerging concepts and potential therapies. Sheller, J.R. *American Journal of the Medical Sciences* 1987; **293:** 298.

The place of high-dose inhaled corticosteroids in ashtma therapy. Smith, M.J. *Drugs* 1987; **33:** 423.

Preoperative identification and evaluation of the patient with lung disease. Tisi, G.M. *Medical Clinics of North America* 1987; **71:** 399.

Central nervous system

Physiology

Central serotonin receptors: effector system, physiological roles and regulation. Conn, P.J., Sanders-Bush, E. *Psychopharmacology* 1987; **92:** 267.

The role of joint receptors in human kinaesthesia when intramuscular receptors cannot contribute. Ferrell, W.R., Gandevia, S.C., McCloskey, D.I. *Journal of Physiology* 1987; **386:** 63.

Evoked potential monitoring during aneurysm operation: observations after fifty cases. Friedman, W.A., Kaplan, B.L. *et al. Neurosurgery* 1987; **20:** 678.

General sleep apnea and partial obstruction of the upper airway. Guilleminault, C., Quera-Salva, M.A. *et al. Annals of Neurology* 1987; **21:** 465.

A comparison of the effects of two inhibitors on brain cholinesterase. Hallak, M., Giacobini, E. *Neuropharmacology* 1987; **26:** 521.

The role of insulin resistance in the pathogenesis of myotonic muscular dystrophy. Hudson, A.J., Huff, M.W. *et al. Brain* 1987; **110** (Part 2): 469.

Manipulating the dopaminergic system in Parkinson's disease. Lang, A.E. *Pharmacology and Therapeutics* 1987; **32:** 51.

Neurotoxins, parkinsonism and Parkinson's disease. Langston, J.W., Irwin, I., Ricaurte, G.A. *Pharmacology and Therapeutics* 1987; **32:** 19.

Repeated atypical neuroleptic administration: effects on central dompamine metabolism monitored by *in vivo* voltammetry. Maidment, N.T., Marsden, C.A. *European Journal of Pharmacology* 1987; **136:** 141.

Disorders of the autonomic nervous system. Part I. Pathophysiology and clinical features. McLeod, J.G., Tuck, R.R. *Annals of Neurology* 1987; **21:** 419.

Sodium channel gating currents. Origin of the rising phase. Stimers, J.R., Benzanilla, F., Taylor, R.E. *Journal of General Physiology* 1987; **89:** 521.

Treatment and medication

Anticholinergic prophylaxis of acute haloperidol-induced dystonic reactions. Boyer, W.F., Bakalar, N.H., Lake, C.R. *Journal of Clinical Psychopharmacology* 1987; **7:** 164.

Pharmacotherapy in spinal cord injury: a critical review of recent developments. Faden, A.I. *Clinical Neuropharmacology* 1987; **10:** 193.

Successful treatment of acute mountain sickness with dexamethasone. Ferrazzini, G., Maggiorini, M. *et al. British Medical Journal* 1987; **294:** 1380.

Treatment of myotonia. Leading article. *Lancet* 1987; **1:** 1242.

Contribution of CSF and vascular factors to elevation of ICP in severely head-injured patients. Marmarou, A., Maset, A.L. *et al. Journal of Neurosurgery* 1987; **66:** 883.

Preoperative management of the surgical patient with neurologic disease. MERLI, G.J., BELL, R.D. *Medical Clinics of North America* 1987; **71**: 511.

Effects of dexamethasone in primary supratentorial intracerebral hemorrhage. POUNGVARIN, N., BHOOPAT, W. *et al. New England Journal of Medicine* 1987; **316**: 1229.

Cerebral hyperperfusion following carotid endarterectomy. SCHROEDER, T., SILLESEN, H. *et al. Journal of Dental Research* 1987; **66**: 824.

Taurine improves the recovery of neuronal function following cerebral hypoxia: an *in vitro* study. SCHURR, A., TSENG, M.T. *et al. Life Sciences* 1987; **40**: 2059.

Treatment of neuroleptic malignant syndrome with dopamine hydrochloride: a case report. UNGVARI, G.A. *Pharmacopsychiatry* 1987; **20**: 120.

Successful improvement of blood pressure, cardiac output, and spinal cord blood flow after experimental spinal cord injury. WALLACE, M.C., TATOR, C.H. *Neurosurgery* 1987; **20**: 710.

The predictive value of catecholamines in assessing outcome in traumatic brain injury. WOOLF, P.D., HAMILL, R.W. *et al. Journal of Neurosurgery* 1987; **66**: 875.

Endocrine and metabolic

Physiology

Defective glucose counterregulation after strict glycemic control of insulin-dependent diabetes mellitus. AMIEL, S.A., TAMBORLANE, W.V. *et al. New England Journal of Medicine* 1987; **316**: 1376.

Developmental responses to opioids reveal a lack of effect on stress-induced corticosterone levels in neonatal rats. BAILEY, C.C., KITCHEN, I. *British Journal of Pharmacology* 1987; **91**: 119.

Lack of effect of beta-endorphin on basal or glucagon-stimulated hepatic glucose production *in vitro*. BRUBAKER, P.L., SUN, A., VRANIC, M. *Metabolism* 1987; **36**: 432.

Stimulation of insulin secretion by beta-endorphin (1–17 & 1–31). CURRY, D.L., BENNETT, L.L., LI, C.H. *Life Sciences* 1987; **40**: 2053.

Kinetics of insulin disappearance from plasma in cortisone-treated normal subjects. ELLEMANN, K., THORSTEINSSON, B. *et al. Clinical Endocrinology* 1987; **26**: 623.

Intrinsic pulsatility of ACTH release from the human pituitary *in vitro*. GAMBACCIANI, M., LIU, J.H. *et al. Clinical Endocrinology* 1987; **26**: 557.

Presynaptic effects of glucocorticoids on dopaminergic and cholinergic synaptosomes—implications for the rapid endocrine–neural interactions in stress. GILAD, G.M., RABEY, J.M., RABEY, V.H. *Life Sciences* 1987; **40**: 2401.

Preliminary report: natriuretic effect of calcium supplementation in hypertensive woman over forty. GILLILAND, M., ZAWADA, E.T. *et al. Journal of the American College of Nutrition* 1987; **6**: 139.

Hyperglycemia and obesity as determinants of glucose, insulin, and glucagon responses to beta-endorphin in human diabetes mellitus. GIUGLIANO, A., SALVATORE, T. *et al. Journal of Clinical Endocrinology and Metabolism* 1987; **64**: 1133.

Biotransformation of caffeine by microsomes from human liver. Kinetics and inhibition studies. GRANT, D.M., CAMPBELL, M.E. *et al. Biochemical Pharmacology* 1987; **36**: 1251.

Circulating somatostatin—physiological regulator of pancreatic function. GYR, K., BEGLINGER, C. *et al. Journal of Clinical Investigation* 1987; **79**: 1595.

Intrarenal and intracellular distribution of renin and angiotensin. HACKENTHAL, E., METZ, R. *et al. Kidney International* 1987; **31** (Suppl. 20): S4.

Atrial natriuretic factor and exocrine pancreas: effects on the secretory process. HEISLER, S., KOPELMAN, H. *et al. Pancreas* 1987; **2**: 243.

Modulation of the effect of acetylcholine on insulin release by the membrane potential of β cells. HERMANS, M.P., SCHMEET, W., HENQUIN, J.C. *Endocrinology* 1987; **120**: 1765.

Plasma concentrations of immunoreactive-atrial natriuretic polypeptide in patients on hemodialysis. KOJIMA, S., INOUE, I. *et al. Nephron* 1987; **45**: 45.

Role of stress in the exacerbation of chronic illness: effects of clonidine on blood pressure, norepinephrine, cortisol, growth hormone and prolactin. LECHIN, F., VAN DER DIJS, B. *et al. Psychoneuroendocrinology* 1987; **12**: 117.

Overview: physiology of renin. LEDINGHAM, J.G.G. *Kidney International* 1987; **31** (Suppl. 20): S49.

Enhanced prednisolone elimination: a possible cause for failure of glucocorticoid therapy in Graves' ophthalmopathy. LEGLER, U.F. *Hormone and Metabolic Research* 1987; **19**: 168.

Minireview: a second look at the second messenger hypothesis. LICHTSTEIN, D., RODBARD, D. *Life Sciences* 1987; **40**: 2041.

Prolonged disruption of plasma beta-endorphin dynamics after trauma in the nonhuman primate. MCINTOSH, T.K. *Endocrinology* 1987; **120**: 1734.

Additive effects of growth hormone releasing factor and insulin hypoglycaemia on growth hormone release in man. PAGE, M.D., KOPPESCHAAR, P.F. *et al. Clinical Endocrinology* 1987; **26**: 589.

Regional differences in brain glucose content in graded hypoglycemia. PASCHEN, W., SIESJO, B.K. *et al. Neurochemical Pathology* 1986; **5**: 131.

Altered hepatic vasopressin and alpha 1-adrenergic receptors after chronic endotoxin infusion. ROTH, B.L., SPITZER, A. *American Journal of Physiology* 1987; **252** (Part I): E699.

Control of renal renin release. STELLA, A., ZANCHETTI, A. *Kidney International* 1987; **31** (Suppl. 20): S89.

Non-ketotic hyperglycinaemia: clinical and biochemical aspects. Tada, K., Hayasaka, K. *European Journal of Pediatrics* 1987; **146:** 221.

Cachectin/tumor necrosis factor induces lethal shock and stress hormone responses in the dog. Tracey, K.J., Lowry, S.F. *et al. Surgery, Gynecology and Obstetrics* 1987; **164:** 415.

Atrial natriuretic peptide and other vasoactive hormones in nephrotic syndrome. Tulassay, T., Rascher, W. *et al. Kidney International* 1987; **31:** 1391.

Characterization of the state of body fluids in anuric hyperglycemic humans. Tzamaloukas, A.H. *Mineral and Electrolyte Metabolism* 1987; **13:** 126.

Determinants of osmotic phenomena created by an isolated change in extracellular solute in anuria. Tzamaloukas, A.H., Kyner, W.T., Galey, W.R. *Mineral and Electrolyte Metabolism* 1987; **13:** 117.

The effects of arginine-8 vasopressin on blood vessels supplying the cerebral cortex. Webb, A.C., Ebenezer, I.S., Burns, B.D. *Regulatory Peptides* 1987; **17:** 257.

Congenital adrenal hyperplasia. Part 1. White, P.C., New, M.I., Dupont, B. *New England Journal of Medicine* 1987; **316:** 1519.

Vasopressin-containing and vasopressin-deficient subpopulations of corticotropin-releasing factor axons are differentially affected by adrenalectomy. Whittnall, M.H., Key, S., Gainer, H. *Endocrinology* 1987; **120:** 2180.

Treatment and medication

Surgery in patients with endocrine dysfunction. Goldman, D.R. *Medical Clinics of North America* 1987; **71:** 499.

Serum osmolality gap in postoperative patients in intensive care. Inaba, H., Hirasawa, H., Mizuguchi, T. *Lancet* 1987; **1:** 1331.

Augmentation by aprotinin of the renal response to vasopressin. Kauker, M.L., Baer, P.G., Nasjletti, A. *Kidney International* 1987; **31:** 1092.

Effects of continuous subcutaneous insulin infusion and intensified conventional therapy on peripheral and autonomic nerve dysfunction. Kronert, K., Hulser, J. *et al. Journal of Clinical Endocrinology and Metabolism* 1987; **64:** 1219.

Beta-endorphin infusion fails to modulate the hormonal and metabolic response to surgery. Lacoumenta, S., Yeo, T.H. *et al. Clinical Endocrinology* 1987; **26:** 657.

Hyperkalemia as a complication of drug therapy. Rimmer, J.M., Horn, J.F., Gennari, F.J. *Archives of Internal Medicine* 1987; **147:** 867.

Diuretics. Rose, B.D., Turka, L.A. In: Kaplan, N.M. *et al.*, eds. *Kidney in hypertension.* New York: Raven Press, 1987; p. 179.

Pain

Physiology

The neurobiology of facial and dental pain—present knowledge, future directions. Sessle, B.J. *Journal of Dental Research* 1987; **66:** 962.

Treatment and medication

Analgesic effect of alprazolam in patients with chronic, organic pain of malignant origin. Fernandez, F., Adams, F., Holmes, V.F. *Journal of Clinical Psychopharmacology* 1987; **7:** 167.

Fluradoline and aspirin for orthopedic postoperative pain. McQuay, H.J., Carroll, D. *et al. Clinical Pharmacology and Therapeutics* 1987; **41:** 531.

Effective postoperative pain control by preoperative injection of diclofenac. Wuolijoki, E., Oikarinen, V.J. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 249.

Other

Physiology

Leukotrienes. Piper, P.J., Samhoun, M.N. *British Medical Bulletin* 1987; **43:** 297.

An elucidation of the arachidonic acid cascade: discovery of prostaglandins, thromboxane and leukotrienes. Samuelsson, B. *Drugs* 1987; **33:** 2.

Anaesthesia, 1987, Volume 42, pages 1147–1150

Obituaries

Barnsley, Arnold, MB, MD, BChir, MRCS, LRCP, FFARCS, DA. Fellow of the Association of Anaesthetists of Great Britain and Ireland. Qualified from Cambridge University in 1934.

Challenger, John Henry, TD, MB, CHB, FFARCS, DA. Formerly Consultant Anaesthetist to the United Bristol Hospitals and latterly a specialist in anaesthesiology and pain relief in Aarhus, Denmark. Qualified from Bristol University in 1942.

Downing, Desmond, MB, BCH, BAO, DObst, RCOG, DA. Formerly Honorary Consultant Anaesthetist, Antrim Health District. Qualified from the University of Belfast in 1949.

Hargadon, John Joseph, MB, ChB, FFARCS, DA. Formerly Consultant Anaesthetist at the Liverpool Royal Infirmary. Qualified from Liverpool University in 1941.

Lake, Roger Harold Nicholas, MB, BS, MRCS, LRCP, FFARCS, DA. Formerly Consultant Anaesthetist in Plymouth. Qualified from London University in 1946.

Mather, Leonard, MRCS, LRCP, FFARCS, DA. Formerly Senior Consultant Anaesthetist at the War Memorial Hospital, Scunthorpe. Qualified from Manchester University in 1923.

Merlin, Paul Tudor, MB, ChB, MRCS, LRCP, FFARCS, DA. Formerly Consultant Anaesthetist to the Portsmouth Group of Hospitals. Qualified from Birmingham University in 1930.

Patterson, William John, MB, BCH, BAO, FFARCS. Formerly Consultant Anaesthetist to the United Sheffield Hospitals. Qualified from the Queen's University Medical School, Belfast in 1927.

Spratt, Leslie William, MA, MB, BChir, MRCS, LRCP, DA. Qualified from the University of Cambridge in 1934.

Steen, Terence Ross, MB, BChir, FFARCS, DA. Formerly Consultant Anaesthetist at Southmead Hospital, Bristol. Qualified from Cambridge University in 1943.

Steward, Anthony Malcolm, MB, BS, FRCS, MRCS, LRCP, DO, DLO, DA. Formerly part-time Associate in the University Department of Surgery, St. Vincent Hospital, Melbourne, Australia. Qualified from London University in 1962.

Thomas, Richard Thomas, LRCP, LRCS, FFARCSI. Formerly Honorary Consultant Anaesthetist at Bronglais Hospital, Aberystwyth. Qualified from the University of Edinburgh in 1944.

International congress calendar

1987

10–14 October. Atlanta, Illinois. *Annual Meeting, American Society of Anesthesiologists.*
Information: John Andes, Esq., 515 Busse Highway, Park Ridge, Illinois 60068, USA.

16–18 October. Toronto, Canada. *Paediatric Anaesthesia Conference.*
Information: Paediatric Anaesthesia Conference, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada.

22 October. Seoul, Korea. *9th Korean–Japanese Symposium and 32nd Annual Congress, Korean Society of Anesthesiologists.*
Information: Professor Jong-Rae Kim, Korean Society of Anesthesiologists, Room 607, Korean Medical Association Building, Seoul, Korea.

22–24 October. Posnan, Poland. *Symposium—DYDAKTYKA '87.*
Information: The Organizing Committee of Symposium DYDAKTYKA '87, Institute of Anaesthesiology and Intensive Therapy, ul. Przybyszewskiego 49, 60-355 Poznan, Poland.

22–24 October. Oslo, Norway. *Annual Meeting of the Norwegian Society of Anaesthetists.*
Information: Dr Svein Sunde, Anestesi Avd., Ulleval Hospital, 0407 Oslo, Norway.

22–24 October. Berlin, Federal Republic of Germany. *2nd International Steglitz Symposium.*
Information: Priv.-Doz. Dr K. Reinhart, Klinikum Steglitz, Freie Universitat Berlin, Hindenburgdamm 30, 1000 Berlin 45, Federal Republic of Germany.

24–30 October. Caracas, Venezuela. *XIX Latino Americano, XIV Asamblea CLASA, XII Congreso Venezolana.*

Information: Dr Carmelo Moreno A., c/o Venezolana An, Av. Jose.Vargas, Ed. Torre del Colegio, Piso 15 Of.D, Urb. Santa Fe Norte, Caracas 1080, Venezuela.

25 October. Lusaka, Zambia. *Annual General Meeting of the Zambian Society of Anaesthesiologists.*
Information: Dr L.N. Chansa, Department of Anaesthesia, University Teaching Hospital, Box 50001, Lusaka, Zambia.

30–31 October. Budapest, Hungary. *Refresher Course.*
Information: Dr Maria Janecsko, Szabolcs u 35, 1135 Budapest, Hungary.

30 October–1 November. Washington, DC. *International Symposium on the Pediatric Airway.*
Information: Dr Lawrence M. Borland, Department of Anesthesia, Children's Hospital of Pittsburgh, One Children's Place, 3705 Fifth Avenue at DeSoto Street, Pittsburgh, Pennsylvania 15213-3417, USA.

1–6 November. Rio de Janeiro, Brazil. *XXXIV Brazilian Congress.*
Information: Dr Jose Carlos F. Maia, R. Rita Ludolf 16 Apto. 102, 22.440 Rio de Janeiro RJ, Brazil.

4–5 November. Baltimore, Maryland. *Progress in in vitro Toxicology.*
Information: Jeanne Ryan, Program Coordinator, Office of Continuing Education, The Johns Hopkins Medical Institutions, 720 Rutland Avenue, Baltimore, Maryland 21205, USA.

5–7 November. Oporto, Portugal. *International Meeting on Anaesthesia and Intensive Care.*
Information: Anaesthesia Department, Hospital S. Joao, Oporto, Portugal.

7–8 November. Mount Sinai Medical Center, New York. *Bernard H. Eliasberg Memorial Symposium: The Cardiac Patient for Non-Cardiac Surgery—The Experts Opine.*
Information: Department of Anesthesiology, Mount Sinai Medical Center, 1 Gustave L. Levy Place, Box 1010, New York, New York 10029, USA.

8–13 November. Caracas, Venezuela. *III Panamerican and Iberic Congress on Intensive and Critical Care Medicine.*
Information: Sociedad Venezolana de Medicina Critica, Colegio Medico del Edo. Miranda, Calle Ele Golf, Quinta La Setenta y Seis, Caracas, Venezuela (P.O. Box 68.625, Altamira, Caracas 1062).

11 November. Prague, Czechoslovakia. *Advances in Pain Therapy Symposium.*
Information: Dr J. Drabkova, Institute of Anaesthesia, Vuvalu 84 15112, Praha 5 Motol, Czechoslovakia.

11–16 November. Guangzhou, People's Republic of China. *Anaesthesia China '87.*
Information: Anaesthesia China '87, International Conference Consultants Ltd, 1st Floor, 57 Wyndham Street, Central, Hong Kong.

12–14 November. Helsinki, Finland. *Annual Meeting of the Finnish Society of Anaesthesiologists.*
Information: Dr Liisa Kaukinen, Inkerink 14, SF-33730 Tampere 73, Finland.

14–15 November. Medical Faculty of Erasmus University, Rotterdam, The Netherlands. *International Symposium on Surfactant Replacement Therapy.*
Information: Dr B. Lachmann, Department of Anesthesiology, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

15–19 November. Rosario, Argentina. *II Congreso Dolor.*
Information: Dr Luis Fiscella, 3 de Febrero 3844, 2000 Rosario, Argentina.

16–20 November. Rotterdam, The Netherlands. *4th International Symposium on Applied Physiology in Cardio Respiratory Emergencies.*
Information: Omar Prakash, MD, Erasmus University, Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

24–28 November. Trieste, Italy. *2nd Postgraduate Course on Recent Advances in Anaesthesia, Intensive Care and Pain Therapy.*
Information: Elisa Malutta, Organizing Secretariat, Trieste Traduzioni Congressi, V. le XX Settembre 4, 34125 Trieste, Italy.

26–28 November. Vina del Mar, Chile. *XV Congreso Chileno.*
Information: Dra Ana Munoz Notari, MAC-IVER 721, Of. 4 Casilla 639, Santiago, Chile.

28 November. Brussels, Belgium. *General Statutory Assembly of the Belgium Society of Anaesthesiologists.*
Information: Professor F. Camu, AZ.VUB Laarbeeklaan 101, B-1090 Brussels, Belgium.

1–4 December. Cairo, Egypt. *2nd Pan Arab Congress.*
Information: Progessor H. Shaker, P.O. Box 71, Dokki Jezza, Cairo, Egypt.

5–7 December. La Paz, Bolivia. *Jornadas: Boliviana.*
Information: Dr Rodolfo Suarez, Sociedad Boliviana de Anestesiologia, Casilla 10015, La Paz, Bolivia.

13–17 December. New York City, USA. *40th Postgraduate Assembly in Anesthesiology.*
Information: Mr Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists, Inc., 30 East 42nd Street, Suite 1501, New York, New York 10017, USA.

19–26 December. Marriott's Mark Resort, Vail, Colorado. *Current Issues in Medicine.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

21–23 December. New Delhi, India. *VIII Australiasian and IX National Conference on Critical Care Medicine and Emergency Disaster Medicine.*
Information: Professor N.P. Singh, Convenor, 147 North Avenue, New Delhi, 11001, India.

1988

3 January–6 February. Marriott's Mark Resort, Vail, Colorado. *14th Annual Vail Conference in Anesthesiology.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

16–23 January. Cancum, Mexico. *Advances in Anesthesiology Symposium.*
Information: Ms Francine Kurth, Department of Anesthesiology, Mount Sinai Medical Center, 1 Gustave L. Levy Place, New York, New York 10029, USA.

22–23 January. Maastricht, The Netherlands. *40th Anniversary of the Netherlands Society of Anaesthesiologists.*
Information: Dr A.E.E. Meursing, Tafelberg 88, 3328 ST Dordrecht, The Netherlands.

6–13 February. Marriott's Mark Resort, Vail, Colorado. *13th Annual Vail Symposium in Intensive Care.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

7–11 February. Sheraton Waikiki Hotel, Waikiki, Hawaii. *16th Obstetric Anesthesia Conference.*
Information: Arlene Rogers, The Ohio State University, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

5–9 March. Hotel Inter-Continental, San Diego, California. *62nd Congress of the International Anesthesia Research Society.*
Information: Dr Emerson A. Moffitt, Executive Secretary, International Anesthesia Research Society, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

12–19 March. Doubletree Lodge, Vail, Colorado. *8th Medical Monitoring Technology Conference.*
Information: Arlene Rogers, The Ohio State University, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

26–27 March. Hyderabad, India. *4th Annual Conference of the Indian Society for Study of Pain.*
Information: Dr Rupendra Lal, Organising Secretary, 3-6-23 Basir Bagh, Hyderabad-500029, India.

27–31 March. The Lodge at Vail, Vail, Colorado. *15th Neonatal and Infant Respiratory Symposium.*
Information: Arlene Rogers, The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

5–8 April. Nottingham. *Junior Anaesthetists' Group Annual Meeting.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

23–27 April. Miami, Florida. *Miami Comprehensive Review Course in Anesthesiology.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

1–6 May. Brisbane, Australia. *Annual Scientific Meeting of the Faculty of Anaesthetists and Royal Australian College of Surgeons.*
Information: Administrative Officer, Faculty of Anaesthetists, RACS Spring Street, Melbourne 3000, Australia.

11–13 May. Sydney, Australia. *5th International Dental Congress on Modern Pain Control.*
Information: Australian Convention and Travel Services (ACTS), P.O. Box 1929, Canberra, ACT 2601, Australia.

16–19 May. Cancum, Mexico. *1st International Symposium of Quantitative Anaesthesia.*
Information: Dr R. Samayoa de Leon, 18 av. "B" 0-03, Zona 15, Ciudad Guatemala, Guatemala, CA, Mexico.

16–20 May. San Diego, California. *Computing in Anesthesia and Intensive Care.*
Information: Miss Robie Brien, Department of Anesthesia (125), 3350 La Jolla Village Drive, San Diego, California 92161, USA.

22–28 May. Washington, DC. *9th World Congress of Anaesthesiology.*
Information: American Society of Anesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

3–4 June. La Villette International Conference Center, Paris, France. *MAPAR 1988.*
Information: Secretariat, MAPAR, Departement d'Anesthesiolgie, Hopital de Bicetre, 78 rue du General Leclerc, F-94275, Le Kremlin-Bicetre Cedex, France.

14–18 June. Baveno-Stresa, Lago Maggiore, Italy. *4th European Congress on Intensive Care Medicine.*
Information: Organizing Secretariat, MGR, Piazza S. Ambrogio, 16, 20123 Milan, Italy.

25–29 June. Halifax, Nova Scotia. *Canadian Anaesthetists' Society Annual Meeting.*
Information: Dr G. Houle, 187 Gerrard Street E, Toronto, Ontario M5A 2E5, Canada.

7–10 September. Rome, Italy. *10th Annual Meeting of the European Academy of Anaesthesiology.*
Information: EAA Secretariat, Instituto Anestesiologia, Univ. Cattolica S. Cuore, Largo A Gemelli 8, 00186 Rome, Italy.

10–14 September. Florence, Italy. *3rd International Symposium.*
Information: Professor M. Zoppi, Cespri Fondazione Pro Juventute, Via Imprunetana 124, 500200 Monteriolo, Florence, Italy.

14–17 September. Brussels, Belgium. *5th International Congress.*
Information: Professor F. Camu, AZ.VU, Laarbeeklaan 101, B-1090 Brussels, Belgium.

15–16 September. Southampton. *Annual Scientific

Meeting, Association of Anaesthetists of Great Britain and Ireland.
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

1 October. Pavia, Italy. *National Congress, Societa Italiana di Anest, Rianimazione e Terapia Intensiva.*
Information: Dr G. Conti, SIARRTI, Universita degli Studi, La Sapienza di Roma, Viale del Policlinico, 00161 Roma, Italy.

8–12 October. San Francisco, California. *Annual Meeting of the American Society of Anesthesiologists.*
Information: John W. Andes, Executive Secretary, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

13–15 October. Mainz, Federal Republic of Germany. *7th Annual Meeting of the European Society of Regional Anaesthesia.*
Information: Klinikum fur Anasthesiologie, Postfach 3960, Langenbeckstrasse 1, 6500 Mainz, Federal Republic of Germany.

23–28 October. Rio de Janeiro, Brazil. *World Congress of Gynecology and Obstetrics.*
Information: Professor Paulo Belfort, Av. Armando Lombardi, 800/223 Barra de Tijuca, 22600 Rio de Janeiro RJ, Brazil.

29 October–2 November. Ballarat, Victoria, Australia. *Annual General Meeting, Australian Society of Anaesthetists.*
Information: The Secretariat, ASA, P.O. Box 600, Edgecliff, NSW 2027, Australia.

6–11 November. Pendiente, Brazil. *XXXV Brazilian Congress of Anaesthesiology.*
Information: Soc. Brazilene Anest., Rua Prof. Alfredo Gomez 36 CEP-22251, Rio de Janeiro RJ, Brazil.

9–12 November. Tauranga, New Zealand. *Conference of Anaesthetists of New Zealand.*
Information: Dr M. Hugel, Conference Secretary, Department of Anaesthetics, Tauranga Hospital, Private Bag, Tauranga, New Zealand.

1989

May. Beograd, Yugoslavia. *VI National Congress of the Yugoslav Society of Anaesthesiologists.*
Information: Dr Nikola Jovanovic, Institut za Radiolog. i Onkolog., 11-000 Beograd Pasterova 14, Yugoslavia.

26–30 June. Copenhagen, Denmark. *20th Scandinavian Congress.*
Information: Professor S.H. Johansen, Herlev Hospital, DK 2730 Herlev, Denmark.

12–16 August. Christchurch, New Zealand. *Combined Meeting, New Zealand Society of Anaesthetists and Australian Society of Anaesthetists.*
Information: The Secretariat, ASA, P.O. Box 600, Edgecliff, NSW 2027, Australia.

1–4 September. Tunisia. *3rd Pan Arab Congress on Anaesthesia and Intensive Care.*
Information: Dr Jamal Al-Shanableh, P.O. Box 15404, Marka-Amman, Jordan.

3–8 September. Kyoto, Japan. *Fifth World Congress on Intensive and Critical Care Medicine.*
Information: The Fifth World Congress on Intensive and Critical Care Medicine, c/o Japan Convention Services Inc., Nippon Press Center Building, 2-2-1 Uchisaiwai-cho, Chiyoda-ku, Tokyo 100, Japan.

14–15 September. Osaka, Japan. *4th International Symposium of Endocrinology in Anaesthesia and Surgery.*
Information: Department of Anesthesiology, University of Hirosaki, School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori-ken 036, Japan.

26–28 September. Swansea. *Annual Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1 3RA.

1990

9–15 September. Warsaw, Poland. *VIIIth European Congress of Anaesthesiology.*
Information: The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o Polish Society of Anaesthesiology and Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

1992

14–19 June. The Hague, The Netherlands. *10th World Congress of Anaesthesiology.*
Information: Dr Harm Lip, Nilantsweg 99, 8041 AR Zwolle, The Netherlands.

Anaesthesia, 1987, Volume 42, pages 1151–1152

Courses in Anaesthesia

Supplementary list (see also *Anaesthesia* 1987; **42**: 1037–42)

The information below is believed to be accurate but those intending to attend a course should check the details with the relevant organiser. Applications and further information cannot be provided by *Anaesthesia*.

FFARCS Part 1

LEICESTER University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW	18–22 January 1988, One-week whole time revision course	NO FEE FOR DOCTORS WITHIN TRENT REGION	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW *Tel.* 0533 541414 *ext.* 474

FFARCS Part 2

LEICESTER University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW	9 October 1987 to 22 April 1988, Half-day release course (Friday afternoons)	NO FEE	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW *Tel.* 0533 541414 *ext.* 474

FFARCS Part 3

LEICESTER University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW	25–29 April 1988, One-week whole time revision course	£35 NO FEE FOR DOCTORS WITHIN TRENT REGION	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW *Tel.* 0533 541414 *ext.* 474
LONDON Department of Anaesthesia, The Royal Free Hospital, Pond Street, Hampstead, London NW3 1QG	April/May and December, Intensive 5-day revision course including simulated exam papers and orals	£100	The Secretary, Department of Anaesthesia, Royal Free Hospital, Pond Street, Hampstead, London NW3 2QG *Tel.* 01 794 0500

Other courses

LONDON Royal Postgraduate Medical School, Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, Goldhawk Road, London W6 0XG	18–20 November 1987, Course in obstetric anaesthesia and analgesia	£125	Symposium Secretary, RPMS, Institute of Obstet and Gynaecology, Queen Charlotte's Materni Hospital, Goldhawk Road, London W6 0XG *Tel.* 01 740 3904
Department of Anaesthesia, St. George's Hospital, Lanesborough Wing, Blackshaw Road, London SW17 0QT	Short courses for up to three people at a time are available, for neurosurgical, cardiac, maxillo-facial and dental anaesthesia, throughout the year	NO FEE	The Secretary, Department of Anaesthesi St. George's Hospital, Blackshaw Road, London SW17 0QT *Tel.* 01 672 1255

Notice

The Royal Society of Medicine

Professor Emeritus W.W. Mushin, CBE, DSc, FRCS, FFARCS, was presented by the President of the Society of Medicine with the Honorary Fellowship of the Society on 21 July 1987 at the Honorary Fello Ceremony. The significance of this is evident since there is an upper limit of 100 Honorary Fellows. The Anaesthetist Honorary Fellows are Professor Sir Robert Macintosh, Professor Sir Geoffrey Organe and Pro T.C. Gray, CBE. *Anaesthesia* congratulates Professor Mushin.

Erratum

Anaesthesia, 1987, Volume 42, pages 764–766

A laryngoscope adaptor for difficult intubation

S. M. YENTIS

It is regretted that, owing to printer's error, Fig. 2 of this article (p. 765) appears back to front laryngoscope assembly should have a right-handed blade and lateral pivoting occurs as describ the text. The laryngoscope appears in the correct orientation in Fig. 3.

Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
Richard J. Kitz, Emanuel M. Papper, John J. Bonica,
Werner Flacke and A.H. Giesecke, Jr.

Publication: Quarterly
Subscription: Volume 6, 1987
Institutions: £56.00 (UK)/$75.00 (Overseas)

Seminars in Anesthesia will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

From a recent issue

Anesthesia Disasters: Incidence, Causes, and Preventability, *R. L. Keenan*

Oxygen Monitoring in the Operating Room, *J. B. Brodsky*

Oximetry as a Warning of Inadequate Ventilation, *D. A. Paulus*

Capnometry and Capnography: The Anesthesia Disaster Early Warning System, *D. B. Swedlow*

Respiratory Monitoring to Detect and Avoid Anesthetic Disasters: Mass Spectrometry, *M. Lichtiger*

Monitoring of Anesthetic Halocarbons: Self-Contained ('Stand-Alone') Equipment, *C. Whitcher*

Development Directions for Monitoring in Anesthesia, *C. K. Waterson and J. M. Calkins*

The Standard of Care and Where It Comes From, *D. S. Rubsamen*

Coupon

Seminars in Anesthesia

To: Journals Marketing Department
Academic Press Inc. (London) Ltd
24-28 Oval Road
London NW1 7DX, England

Please tick

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.. Name (Capitals) ....

Address ....

.... Date........................

NEW FROM BUTTERWORTHS

The third edition of the definitive textbook on respiratory physiology

Applied Respiratory Physiology

Third Edition

J F Nunn, MD, PhD, FRCS, FFARCS, FFARACS(Hon)
Head of Division of Anaesthesia, Medical Research Council Clinical Research Centre; Honorary Consultant Anaesthetist, Northwick Park Hospital, Middlesex, UK

- ★ **Completely revised**
- ★ **Reorganised into two sections: principles; applications**
- ★ **Many new topics have been added**

August 1987 600 pages 234 × 165 mm Hardcover
Illustrated – 9 half-tones, 191 line and 6 colour photographs
0 407 00342 8 £35.00

Review of all aspects of apparent awareness during general anaesthesia

Consciousness, Awareness and Pain in General Anaesthesia

Edited by **M Rosen,** MBChB, FFARCS
Honorary Professor in Anaesthetics, Department of Anaesthetics, University Hospital of Wales, Cardiff, UK

J N Lunn, MD, FFARCS
Reader in Anaesthetics, University of Wales College of Medicine, Cardiff, UK

- ★ **22 chapters considering the problem from clinical, psychological, physiological and legal points of view**
- ★ **Appendix with verbatim extracts describing the personal experiences of a number of patients**

September 1987 240 pages approx 234 × 165 mm Hardcover
Illustrated – 15 line drawings 0 407 00749 0 £29.50 approx

Please order these titles from your usual bookseller – or in case of difficulty from Butterworths at the address below.

Butterworths
meeting professional needs

[illegible]

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology · Biochemistry, Biology, Botany · Cancer research, Cardiology, Chemistry, Computer science · Economics, Engineering, Environmental science · Food science · Geography, Geology · Immunology · Materials technology, Mathematics, Microbiology · Neuroscience, Nutrition · Oncology, Ornithology · Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology · Religion · Sociology, Speech, Surgery · Toxicology · Virology · Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.   Orlando, FL 32887, USA.

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

Overseas and Associate Membership

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

Junior Membership (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation on the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

Membership Fees (inclusive of the journal *Anaesthesia*)

Ordinary Members: Subscription **£65** (Husband and wife **£50** each)

Overseas and Associate Members: Subscription **£65**

Junior Members: Subsciption **£38** (**£50** after 3 years if still in training)

Retired Members: who receive *Anaesthesia* **£10** (there is no subscription for those who do not).

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(*This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.*)

........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name)... offer my name as a candidate
BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

....

(Signed)..

Address...
....Hospital Tel. No:..
....Home Tel. No:..

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)..
(NAME IN BLOCK LETTERS)
Address...
BLOCK LETTERS

2. (Signed)..
(NAME IN BLOCK LETTERS)
Address...
BLOCK LETTERS

* See the reverse of this page for details of membership categories.
† One sponsor must be an Ordinary Member of the Assocation.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (UK).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence are to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s), degrees and designations should be typed in lower case below the line. Initials should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left-hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

Use the form of reference adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscripts submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooven CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences,* 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the left-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS, ABBREVIATIONS AND STATISTICS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 42, no. 10, October 1987

EDITORIAL

Future organisation of anaesthetic health care
M. Rosen 1043

ORIGINAL ARTICLES

Anaesthetic properties of pregnanolone emulsion. A comparison with alphaxolone/alphadolone, propofol, thiopentone and midazolam in a rat model
S. Høgskilde, J. Wagner, P. Carl and M. Bredgaard Sørensen 1045
Analgesia from morphine and ketamine. A comparison of infusions of morphine and ketamine for postoperative analgesia
H. Owen, R.M. Reekie, J.A. Clements, R. Watson and W.S. Nimmo 1051
A comparison of the early pharmacokinetics of midazolam in pregnant and nonpregnant women
C.M. Wilson, J.W. Dundee, J. Moore, P.J. Howard and P.S. Collier 1057
Intravenous sedation for cataract surgery
J. Gilbert, J.E. Holt, J. Johnston, B.A. Sabo and J.S. Weaver 1063
Local tissue oxygenation following radial artery cannulation
J.M. Murray and A.Mowbray 1070

CASE REPORTS

Cardiac arrest in near-term pregnancy
S.L. Lindsay and G.C. Hanson 1074
Anaphylactoid reactions to prilocaine
K. Ruiz, J.D. Stevens, J.J.A. Train and J. Watkins 1078
A case of prolonged hypotension following intravenous guanethidine block
E. Sharpe, R. Milaszkiewicz and F. Carli 1081

APPARATUS

Closed-loop administration of atracurium. Steady-state neuromuscular blockade during surgery using a computer controlled closed-loop atracurium infusion
N.R. Webster and A.T. Cohen 1085
Monitoring neuromuscular blockade. The table knife transducer
C.R. Dundas, I.D. Levack and M.S. Brockway 1092

HISTORICAL

Sir Ivan Magill. A supplementary bibliography
H.A. Condon 1096

FORUM

An epidural infusion technique for labour
D.G. Gaylard, I.H. Wilson and H.G.R. Balmer 1098
The Triservice anaesthetic apparatus. Trial of isoflurane and enflurane as alternatives to halothane
M. Kocan 1101
Interview method affects incidence of postoperative sore throat
C.J. Harding and F.K. McVey 1104
Antiemetic studies with traditional Chinese acupuncture. A comparison of manual needling with electrical stimulation and commonly used antiemetics
R.G. Ghaly, K.T.J. Fitzpatrick and J.W. Dundee 1108
Unintentional dural puncture. A survey of recognition and management
R.W. Okell and J.S. Sprigge 1110

CORRESPONDENCE 1114

BOOK REVIEWS 1130

ANAESTHETIC LITERATURE 1136

OBITUARIES 1147

INTERNATIONAL CONGRESS CALENDAR 1147

COURSES IN ANAESTHESIA 1151

NOTICE 1152

ERRATUM 1152

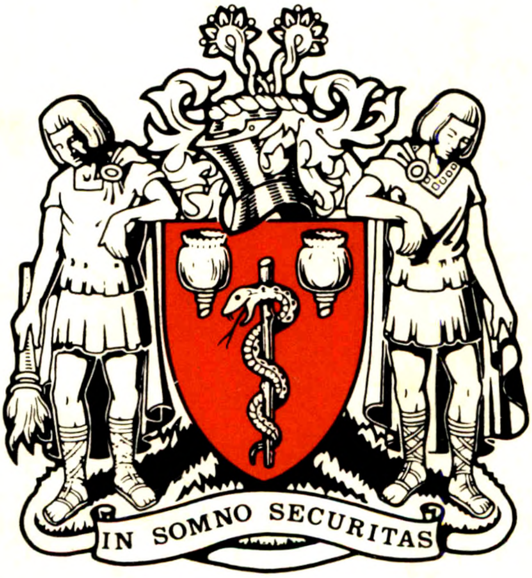
Printed in Great Britain by Richard Clay Ltd, Bungay, Suffolk

Acc
6.4.8

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

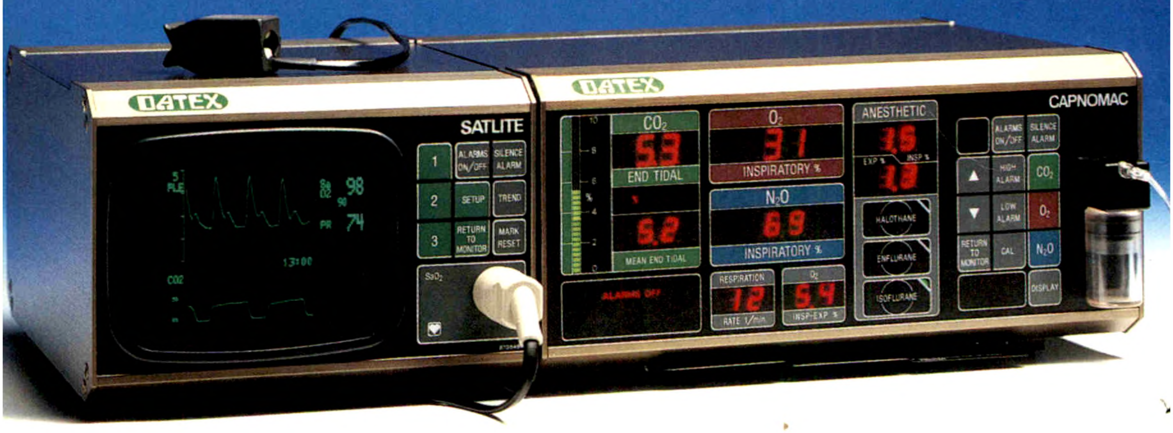
Volume 42 Number 11 November 1987



Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London San Diego New York Berkeley Boston
Sydney Tokyo Toronto

ISSN 0003-2409

Pulse oximetry or multigas monitoring for your operating theatre? Why not both...



SATLITE™ and **CAPNOMAC™**

is an advanced operating theatre pulse oximeter providing SaO_2, pulse rate, the calibrated pulse waveform and trends of all three parameters.

is an anaesthesia agent and airway gas monitor, providing continuous breath-by-breath information on: CO_2, O_2, N_2O and the anaesthetic agent.

TOGETHER

they will provide you with the added bonus of the capnogram and trends of all the gases and the anaesthetic agent – both inspired and expired values.

See just how well SATLITE™ and CAPNOMAC™ together can meet your needs!

Distributed in the UK by:

For people who care

DATEX

Vickers Medical
Priestley Road,
Basingstoke,
Hampshire RG24 9NP, England
Tel. 0256 29141 Telex 858697

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

---

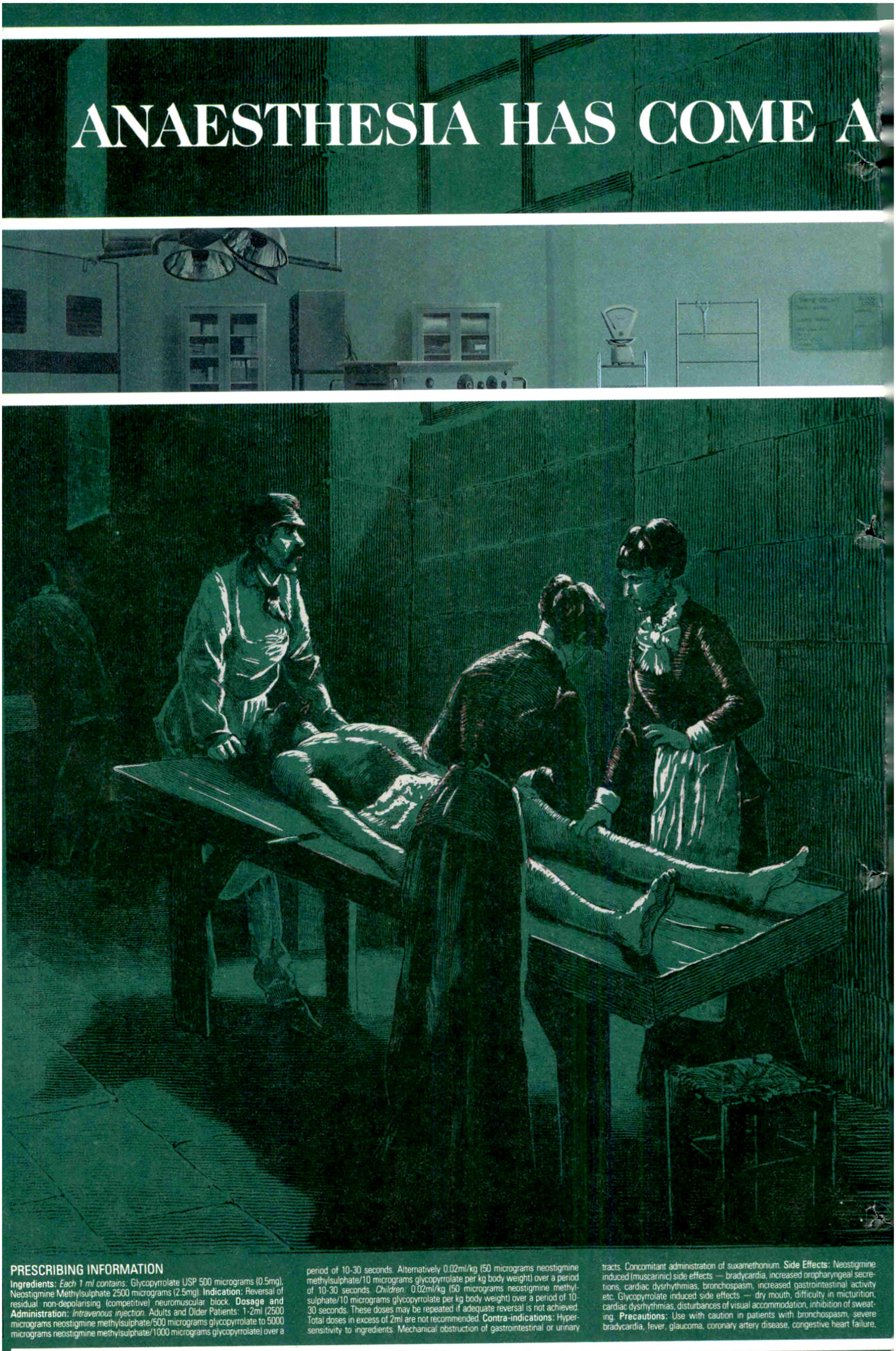
Editor J. N. LUNN
Assistant Editors M. MORGAN, R. GREENBAUM, R. M. JONES, A. R. AITKENHEAD
Editor of *Anaesthesia News* J. N. HORTON
Editorial Board
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
Ex officio
The President of the Association M. ROSEN
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association P. MORRIS
The Immediate Past Honorary Secretary of the Association M. T. INMAN

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee.
A written statement of this acceptance may be requested by the Editor.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Limited for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
1987, Volume 42, 12 issues. Inland £90.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300–0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
U.S. POSTMASTER: send address changes to "Anaesthesia", c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Second class postage paid at Jamaica, New York 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
© 1987 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.
ISSN 0003–2409

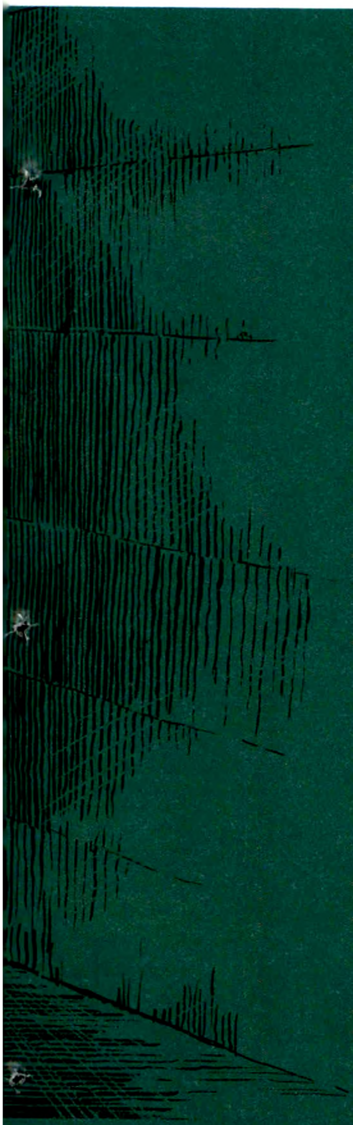


PRESCRIBING INFORMATION

Ingredients: *Each 1 ml contains:* Glycopyrrolate USP 500 micrograms (0.5mg), Neostigmine Methylsulphate 2500 micrograms (2.5mg). **Indication:** Reversal of residual non-depolarising (competitive) neuromuscular block. **Dosage and Administration:** *Intravenous injection.* Adults and Older Patients: 1-2ml (2500 micrograms neostigmine methylsulphate/500 micrograms glycopyrrolate to 5000 micrograms neostigmine methylsulphate/1000 micrograms glycopyrrolate) over a period of 10-30 seconds. Alternatively 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. *Children:* 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. These doses may be repeated if adequate reversal is not achieved. Total doses in excess of 2ml are not recommended. **Contra-indications:** Hypersensitivity to ingredients. Mechanical obstruction of gastrointestinal or urinary tracts. Concomitant administration of suxamethonium. **Side Effects:** Neostigmine induced (muscarinic) side effects — bradycardia, increased oropharyngeal secretions, cardiac dysrhythmias, bronchospasm, increased gastrointestinal activity etc. Glycopyrrolate induced side effects — dry mouth, difficulty in micturition, cardiac dysrhythmias, disturbances of visual accommodation, inhibition of sweating. **Precautions:** Use with caution in patients with bronchospasm, severe bradycardia, fever, glaucoma, coronary artery disease, congestive heart failure,

A·H·ROBINS

LONG WAY…



…SO HAS REVERSAL

In recent years, many advances have been made in the field of anaesthesia, including reversal of residual neuromuscular blockade.

A. H. Robins has been a major contributor to this area with Robinul, an anticholinergic agent which provides significant advantages over atropine.

Robinul produces less initial tachycardia, and better protection against the peripheral muscarinic effects of neostigmine than atropine. In addition, the quality of recovery after Robinul is better than after atropine, due to limited penetration of Robinul into the central nervous system.

Clinical experience has demonstrated that simultaneous administration of Robinul and neostigmine is associated with greater cardiostability at reversal, than separate injections. This had led A. H. Robins to develop ROBINUL-NEOSTIGMINE injection, a ready prepared mixture containing standard doses of Robinul and neostigmine for reversal, in a 1ml ampoule.

Robinul-neostigmine injection provides dependable and convenient reversal of residual neuromuscular blockade, contributing further towards improvements in anaesthesia.

diac dysrhythmias, hypertension, thyrotoxicosis, epilepsy or Parkinsonism.
e with caution in patients with intestinal anastomoses. Safety in pregnancy/
tation has not been established. **Basic NHS price** £9.40 (10 x 1ml ampoules).
gal Category POM **Package Quantities** Packs of 10 ampoules. **Further**
ormation Robinul Neostigmine Injection can be used when atropine has been
ed as a pre-operative anti-cholinergic. **Product Licence Number** 0100/0099.
oduct Authorisation Number 86/27/1

ROBINUL®
GLYCOPYRROLATE
NEOSTIGMINE
NEOSTIGMINE METHYLSULPHATE

Simonsen and Weel defibrillators are tough – they're also very sophisticated. The latest design (we call it the 700 range) uses patented Zoll non-invasive external pacemaker technology and is the first time that a PACEMAKER and a DEFIBRILLATOR have been available as a single portable unit. With built-in ECG and pacing simulation the equipment has good artefact rejection and offers a stable ECG trace even in difficult environments. Another important and useful feature is the auto-record facility which gives the previous four seconds of cardiac activity, as a print-out, each time the defibrillator is used. All the machines in this new range have the rugged NORYL lightweight casing and have been ergonomically designed with clear graphics for use "under pressure" in emergency conditions. Paediatric paddles are incorporated as standard. The unit is available with charging facilities of 240v or 12 volts for use in hospitals or emergency vehicles.

Find out about our pace setting defibrillators now . . .

S&W Simonsen & Weel Ltd., Ruxley Corner, Sidcup, Kent DA14 5BL. Telex: 896328. Tel: 01-309 0433

Hespan*

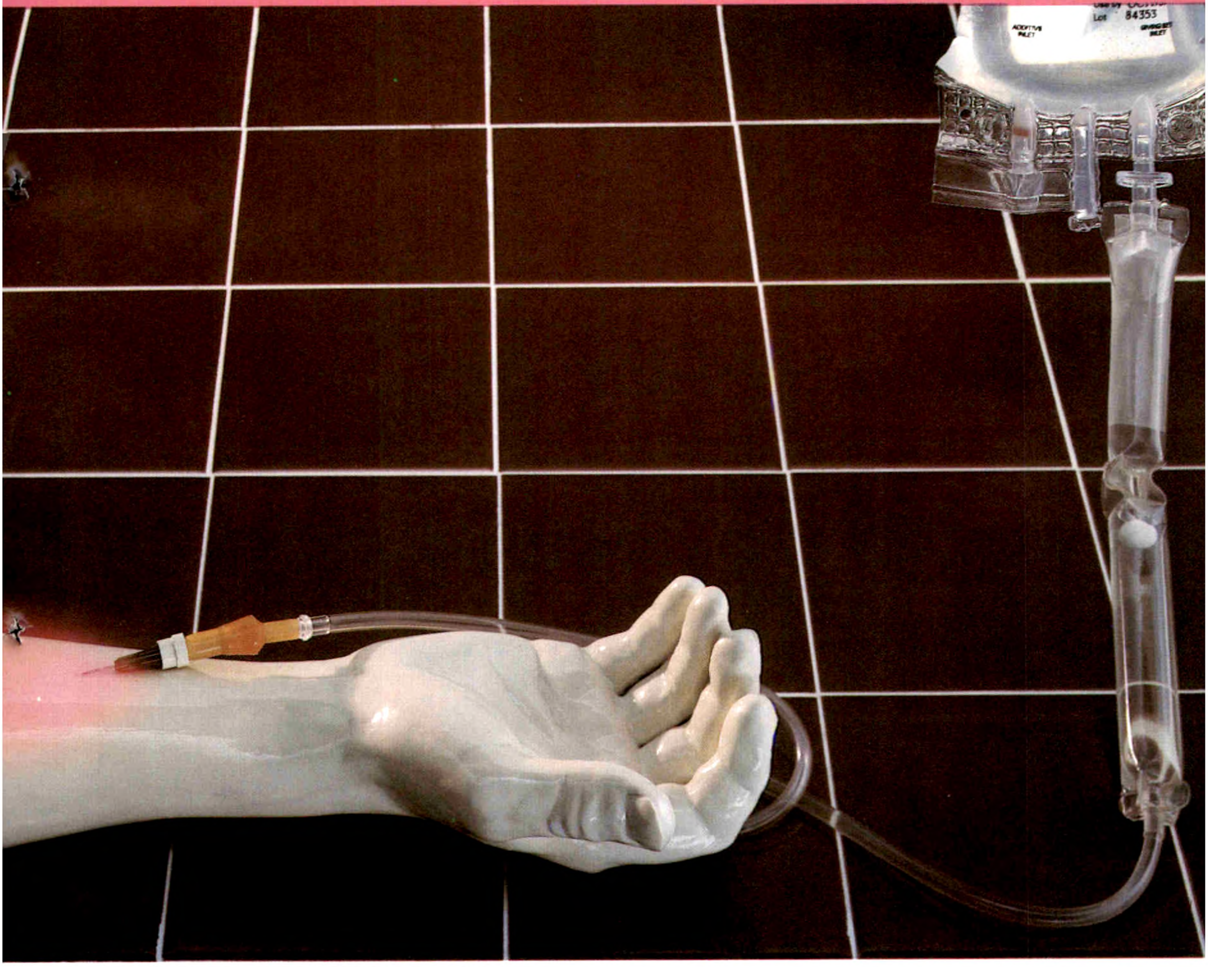
Hetastarch 6%

Controls plasma volume for a full 24 hours

Rapid plasma volume expansion restores cardiac output and tissue perfusion for vital organ function.[1-3]

Reliable increase in colloid osmotic pressure reduces the risk of tissue and pulmonary oedema.[4]

Available freely without dependence on blood donations, without the risk of transmitting disease.



References 1. S. Lazrove, *et al., Crit. Care Med.*, 1980, *8(5).* **2.** V.K. Puri, *et al.* Data on file. **3.** V. Hempel, *et al., Anaesthetist*, 1975, *24*, 198-201. **4.** M.T. Haupt and E.C. Rackow, *Crit. Care Med.*, 1982, *10*, 159-162. For full prescribing information see next page. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel: (0438) 734549.

DU PONT

*Registered trademark

Hespan Prescribing Information

Composition Each 100ml Hespan contains: Hetastarch 6.0g. Sodium Chloride BP 0.9g. Water for injections BP qs, pH adjusted with Sodium Hydroxide. **Indications** 1. As a plasma volume expander in hypovolaemia. 2. Leucapheresis. 3. Extracorporeal circulation. **Contraindications Warnings** There are no absolute contraindications to the use of Hespan. Use with caution in patients with established renal failure. Hespan can produce dilutional effects on fibrinogen and prothrombin activity. In large volumes, Hespan may alter the coagulation mechanism and produce a transient prolongation of the clotting time. Use with caution in patients with severe bleeding disorders. Use with caution in patients vulnerable to vascular overloading. Caution should be observed before administering Hespan to patients with a history of liver disease in view of slightly raised indirect bilirubin levels observed on very rare occasions in volunteers. There is a low incidence of allergic reactions and the administration is not associated with raised plasma histamine levels. Mild peri-orbital oedema, urticaria or wheezing have been reported and are readily controlled by discontinuation of the drug and, if necessary, administration of an antihistamine. **Dosage and Administration—Plasma Volume Expansion** Intravenous infusion only, in an initial volume approximately equal to half the estimated blood loss. In adults the amount usually administered is 500ml to 1,000ml. Total dosage does not usually exceed 1,500ml per day or 20ml per kg of bodyweight for a typical 70kg patient, however the limiting dose will depend on circulating volume and haematocrit. In acute haemorrhagic shock, an initial administration rate approximately 20ml/kg/hr may be recommended, in burns or septic shock, it is usually administered at slower rates. **Leucapheresis** 250-700ml Hespan is typically added to the Y junction just above the bleed out in the ratio of 1 part citrated Hespan to at least 8 parts whole blood, ratios of 1:20 have been used. On rare occasions, 500ml Hespan has been infused into the donors 15-30 minutes before collection. Multiple leucapheresis procedures using Hespan of up to 2 per week or a total of 7-10 have been reported to be safe and effective. The safety of more frequent or a greater number of procedures has not yet been established. **Product Licence Number** 2737/0042. **Package Quantities** Hespan is supplied in 500ml flexible plastic bags. Basic price £16.72. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel. (0438) 734549.

DU PONT

ANESTHESIA AND THE GERIATRIC PATIENT

Edited by
SUSAN WILSON KRECHEL, M.D.

Anesthesia and the Geriatric Patient represents the state of the art in the long-neglected area of anesthetic management of elderly patients. This new book features a collection of the most pertinent and informative topics on the subject. Approximately one-third of the book is devoted to basic science topics on physiology and pharmocology of aging as related to anesthesia practice with the remainder focusing on clinical aspects.

1984, 272pp., $44.50/£37.50
ISBN: 0.8089.1661.0

CLINICAL FEATURES IN ANESTHESIOLOGY

Edited by
JONATHAN L. BENUMOF,
University of California,
San Diego School of Medicine.

A Volume in the ANESTHESIA UPDATE Series

Covering the entire scope of anesthesia from both clinical and basic science perspectives, this comprehensive work presents the latest important developments in anesthesiology. With a concise emphasis on what is really "new" in the field, individual chapters by well-known experts discuss such vital issues as: • recent developments and breakthroughs in pharmocology • anesthesia techniques in operative, pre- and postoperative environments • special topics in the evolution of anesthesia, including a history of anesthesia and future directions • drug abuse in the medical profession.

1983, 288pp., $39.50/£33.00
ISBN: 0.8089.1580.0

Grune and Stratton

ORLANDO, FLORIDA 32887, U.S.A.
24-28 Oval Road, London NW1 7DX,
England

Free loan of educational video

"The pharmacokinetics of drug infusions"

Written and presented by
PROFESSOR
C J HULL
University of Newcastle-upon-Tyne

Another service to
anaesthesia from the
Medical Development
Department of Janssen.

For details of how to
borrow a copy of this video
please contact:-

Joanne Hainge,
Anaesthetists Information Service,
Janssen Pharmaceutical Ltd.,
Grove, Wantage, Oxon, UK.
Telephone: 02357 2966

JANSSEN
PHARMACEUTICAL LIMITED

VYGON

Many speak of Seldinger but . . .

VYGON
124
leader cath
Made in France
Cathéter intravasculaire ORX avec guide métallique (méthode de Seldinger) pour la voie sous-clavière
XRO intravascular catheter with metal spring guide (Seldinger-method) for subclavian introduction
VYGON

Seldinger speaks only of Leader-Cath

Sven-Ivar Seldinger

Vygon (UK) Limited, Bridge Road,
CIRENCESTER, Glos., GL7 1PT.
Telephone: (0285) 67051 Telex: 43342 VYGON G

"Please send me details of the
Leader-Cath range"

Name:
Designation:
Hospital: Ext:
Address:
Telephone:

International symposium on recent developments in muscle relaxation

at The Royal College of Surgeons of England London WC2.
Saturday November 28th, 1987. Registration at 9.30am.

For further information and programme contact Conference Secretariat,
c/o 4 Nicholas Road, Hunters Ride, Henley-on-Thames, Oxon.

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology · Biochemistry, Biology, Botany · Cancer research, Cardiology, Chemistry, Computer science · Economics, Engineering, Environmental science · Food science · Geography, Geology · Immunology · Materials technology, Mathematics, Microbiology · Neuroscience, Nutrition · Oncology, Ornithology · Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology · Religion · Sociology, Speech, Surgery · Toxicology · Virology · Zoology

BOOKS AND JOURNALS

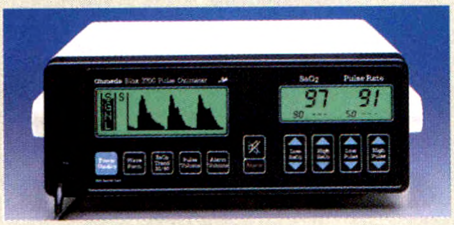
24-28 Oval Road, London NW1 7DX, U.K.   Orlando, FL 32887, USA.

Now there's a whole new way to look at pulse oximetry.

Representational

Ohmeda announces a bright new display.

The Ohmeda Biox 3700 has a bright new LCD that you can really read, three times brighter than before. The panel is easy to see, whether you are standing or sitting, from as far away as 20 feet.



Plus the perfect probe.

The high intensity light source of the new Flex II probe provides a steady, strong signal, able to penetrate variable tissue thickness or pigmentation. Its softer material allows fast, easy application on multiple patient sites. Plus, the economical Flex II is *re-usable* and more flexible, perfect for neonatal and pediatric patients.

Only from Ohmeda—the Company that listens when you talk pulse oximetry.

We're proud to be the original innovators in pulse oximetry. We've been with you from the start—in the OR and in the ICU, in the lab, on your rounds, and in the field for home care. Ohmeda has listened to your ideas and responded to your needs with the exciting new bright display and the revolutionary Flex II *re-usable* probe. And our new software makes the 3700 easy to use on low perfusion patients and during sleep studies. Proof that Ohmeda puts your best and brightest ideas to work, exactly as you envisioned them.

A new display. A new probe. Both ready for you now.

Your Ohmeda representative has the new 3700 and Flex II re-usable probe ready for delivery. Call us today for your complimentary demonstration. With our field sales and service organization located throughout the world, you'll be looking on the bright side of pulse oximetry right away.

Ohmeda

Ohmeda
Elizabeth Way
Harlow, Essex CM 19 5AB
U.K. Sales Telephone 0279 442001
Telex 81497 OHMEDH G
A Division of The BOC Group Inc.
BOC Health Care

Form #E001 © 1987 The BOC Group Inc

Anaesthesia with security

escribing Information: FORANE® (isoflurane) **Indications:** for inhalation anaesthesia. **Dose:** induction should begin at 0.5% and be adjusted propriately. Maintenance concentrations generally lie between 1.0% and 2.5%. Elderly: lesser concentrations normally required. Children: adequate ta are not available in children under two years of age. **Contraindications:** know sensitivity to Forane, or a history of malignant hyperthermia following a vious adminstration. **Side-effects:** hypotension and respiratory depression. Shivering, nausea and vomiting may occur during recovery. **Basic N.H.S. ce:** £33.50 per 100ml. **P.L. Number:** 0037/0115.

Abbott Laboratories Lim
Queenborough, Kent ME1

Anaesthesia, 1987, Volume 42, pages 1153–1155

Editorial

The EEG and awareness during anaesthesia

The transition from wakefulness to sleep, or from alertness to relaxation, is accompanied by a change from low-voltage, fast waves on the electroencephalograph (EEG) to high-voltage, slow waves. A similar change of EEG pattern due to anaesthetics was first reported in 1937 by Gibbs *et al.*,[1] and later related to arterial blood levels by Faulconer and Bickford[2] in 1960. The assessment of level of consciousness during anaesthesia is becoming a problem of paramount importance with the increased popularity of muscle relaxants combined with light planes of anaesthesia. Faulconer and Bickford,[2] however, dealt with a wide range of blood levels of anaesthetics, from the unanaesthetised state to deep levels at which an isoelectric EEG was recorded. Their scale of changes in the EEG, as a result of anaesthetic action, was not suitable for the prediction of awareness during anaesthesia. Further, the difficulty of reading an unprocessed EEG tracing discouraged anaesthetists. The advent of automated EEG processing devices such as power-spectrum analysis, which transform the bizarre EEG oscillation to quantitative indices, renewed anaesthetists' interest.[3] However, this process ironed out the patterns characteristic of individual agents, so curiosity in the mechanism was lost and attention directed to correlation between the processed data and physiological variables. These trials were, however, also unsuccessful and we learnt that an understanding of the mechanism of changes in the EEG is essential for further advances.

The duration of a nerve action potential is roughly a millisecond. Fourier analysis of an EEG does not yield a component of such short-lasting activity, which indicates that the EEG is not the summed oscillation of nerve action potentials. The components of EEG activity last for several tens to hundreds of milliseconds and are found in the synaptic potential of pyramidal cells.[4] These cells are large, located in the 5th layer of the cortex and have a long apical dendrite up to 2 mm in length, which ascends from the cell body through overlying cellular layers and frequently reaches the outermost layer of the cortex. These cells are arranged parallel to one another and perpendicular to the cortical surface. The dendrites of these cells receive inputs of two kinds of thalamocortical projection: the generalised and the specific.[5,6] The generalised projection reflects the wide distribution of the effects of indiscriminate activation, and the specific reflects not only the thalamocortical stages of the afferent systems but all others that project on the cortex in a precise manner, for example, the projection of the nucleus ventralis lateralis on the motor cortex. The ascending reticular activating system lies parallel with, and receives collateral input from, the afferent systems and regulates properly the levels of cell excitability of cortex, basal ganglia and other grey structures.

Electrical stimulation at a rate of 6–12/second, of the nuclei of the generalised thalamocortical projection evokes a peculiar waxing and waning type of cortical response, called the recruiting response. This response is similar to so-called sleep and barbiturate spindle bursts in cortical distribution and waveform, and is most readily produced in a quiet, relaxed or lightly anaesthetised state with barbiturate,[5] halothane and methoxyflurane.[7] This response is reduced in amplitude, or blocked, by arousal stimulation such as high-frequency electric shocks given at the sensory path or the reticular activating system. The present understanding[5–8] is that activation of the generalised thalamic cells produces phasing of their activity, and this phased (i.e. synchronised) activity projects a synchronised output on the apical dendrite of the pyramidal cells. The synchronised depolarisation of the apical dendrites thus produced, is summed to yield high-voltage, slow waves on the EEG. The phasing of this system is suppressed or blocked by arousal stimulation, which gives rise to random activity. When the dendrites are randomly activated, their individual influences on synaptic currents cancel one another and the net result is to produce low-voltage, fast waves on the EEG. The high-voltage, slow EEG of barbiturate anaesthesia and sleep is produced as a result of the phasing of cell firing in

0003–2409/87/111153 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

the generalised thalamic nuclei: a small dose suppresses the activity of the reticular activating system and thus facilitates the phasing of thalamocortical cell activity and, by summation, activities of greater amplitude are produced on the EEG. A large dose, on the other hand, suppresses not only the cell activity of the reticular activating system but that of both the thalamocortical projection system and the pyramidal cells, and total EEG suppression is produced. The total effects of the drug are thus biphasic. Most halogenated anaesthetics, including halothane, have similar neuropharmacological properties: they suppress the cell activity of the reticular activating system in a dose-related manner and produce biphasic effects on the EEG. Further, their EEG patterns are similar to that of barbiturate in cortical distribution and waveform, which indicates that the same neural mechanism is working. We have classed these anaesthetics as CNS depressant.[9]

Another type of rhythmic, slow sine wave (2–6 Hz) EEG is produced by ether, cyclopropane and ketamine.[9] This is in striking contrast to that produced by barbiturates and halogenated anaesthetics and is associated with the activation of neurons in the reticular activating system. Nitrous oxide, when added to barbiturate or halogenated anaesthetics, activates the reticular neurons which are already suppressed by these anaesthetics, and converts the EEG pattern from the barbiturate type to the ether type. Arousal stimulation converts the barbiturate-type slow waves to the ether type in animals anaesthetised with barbiturate, and facilitates the appearance of ether-type slow waves in animals anaesthetised with ether, cyclopropane or ketamine.[10] Noxious stimulation, which undoubtedly stimulates the reticular activating system, converts the barbiturate-type slow waves to the ether type in human infants and children.[11] We have classed these anaesthetics as CNS excitant.[9] This type of slow wave shares some similarity with the barbiturate type, in that it appears synchronously over the whole of both hemispheres, which indicates the presence of some phasing mechanism, possibly in the centro-encephalic structure. No study has ever attempted to prove this.

Implicit in the above view of anaesthetic action is the assumption that brain functions are affected passively by anaesthetic agents. There is also a possibility that the brain reacts actively to a considerable degree. The evidence for this is that the brain develops acute tolerance to the EEG effects of nitrous oxide[9,12,13] and that when the rate of administration varies, the brain yields different EEG patterns at apparently equal blood levels of anaesthetics.[14,15] The former may be related to the development of awareness during nitrous oxide anaesthesia. Nothing is known, at present, of the significance of the latter phenomenon.

Depth of anaesthesia is not necessarily a measure of brain content of anaesthetics but it is a measure of efficiency of performance of brain functions. There is no evidence, but the latter is undoubtedly an outcome of the firing of neurons. It is thus apparent that there is no implicit correlation between the amount of cell firing, as measured, and efficiency of performance; suppression of performance by anaesthetics may be associated either with suppression or with activation of cell firing in the reticular core, depending on the quality of anaesthetic used. Slowing of the EEG represents suppression of the functional performance of the brain but, strictly, this is only an empirical correlation and is not a description of a mechanism. Further, this rule is too simple to apply to measure the subtle, but critical, phase of transition between awareness and unawareness during anaesthesia. Consciousness or awareness is indeed not an all-or-none phenomenon, but a graded state. The assumption that both types of high-voltage, slow-wave EEG are produced by the phasing of cell firing of some neural system, does not necessarily advance our capability to predict awareness since nothing is known at present of the physiological significance of such phasing of cell firing, especially in relation to functional performance. One extremely apposite example in which phasing of cell firing can be postulated, is the case of alpha activity in the EEG. This activity is best obtained in the occipital leads, in the relaxed but fully conscious state, and disappears when brain functions are suppressed by sleep and anaesthesia. If any correlation does exist between the EEG and the higher integrative functions of the brain such as awareness or vigilance, the explanation available at present remains circumstantial.

Department of Anesthesiology,
Kyoto University Hospital,
Sakyo-ku, Kyoto 606, Japan

K. MORI

References

1. GIBBS FA, GIBBS EL, LENNOX WG. Effect on the electro-encephalogram of certain drugs which influence nervous activity. *Archives of Internal Medicine* 1937; **60:** 154–66.
2. FAULCONER A Jr, BICKFORD RG. *Electroencephalography in anesthesiology.* Springfield, Illinois: Thomas, 1960.
3. LEVY WL, SHAPIRO HM, MARUCHAK G, MEATHE E. Automated EEG processing for intraoperative monitoring. A comparison of techniques. *Anesthesiology* 1980; **53:** 223–36.
4. POGGIO GF, MOUNTCASTLE VB. Functional organization of thalamus and cortex. In: MOUNTCASTLE VB, ed. *Medical physiology, Vol. 1,* 14th edn. St Louis: C.V. Mosby, 1980: 271–98.
5. JASPER HH. Unspecific thalamocortical relations. In: MAGOUN HW, ed. *Handbook of physiology. Section 1: Neurophysiology, Vol. 1.* Baltimore: Williams and Wilkins Co., 1960: 1307–21.
6. SASAKI K. Electrophysiological studies on thalamo-cortical projections. *International Anesthesiology Clinics* 1975; **13:** 1–35.
7. MORI K. An experimental study of spindle bursts in electro-encephalogram during inhalation anesthesia. *Far East Journal of Anesthesia* 1964; **4:** 31–42.
8. MOUNTCASTLE VB. Sleep, wakefulness, and the conscious state. In: MOUNTCASTLE VB, ed. *Medical physiology, Vol. 1,* 14th edn. St Louis: C.V. Mosby, 1980: 299–323.
9. MORI K, WINTERS WD. Neural background of sleep and anesthesia. *International Anesthesiology Clinics* 1975; **13:** 67–108.
10. MORI K, KAWAMATA M, MIYAJIMA S, FUJITA M. The effects of several anesthetic agents on the neuronal reactive properties of thalamic relay nuclei in the cat. *Anesthesiology* 1972; **36:** 550–7.
11. OSHIMA E, SHINGU K, MORI K. EEG activity during halothane anaesthesia in man. *British Journal of Anaesthesia* 1981; **53:** 65–72.
12. STEVENS JE, OSHIMA E, MORI K. Effects of nitrous oxide on the epileptogenic property of enflurane in cats. *British Journal of Anaesthesia* 1983; **55:** 145–54.
13. MORI K. Anesthesia and brain functions. *Proceedings of 8th world congress of anaesthesiologists.* Excerpta Medica, 1984: 15–24.
14. AVRAMOV MN, SHINGU K, OMATSU Y, OSAWA M, MORI K. Effects of different speeds of induction with sevoflurane on the EEG in man. *Journal of Anesthesia* 1987; **1:** 1–7.
15. SEO N, OSHIMA E, STEVENS J, MORI K. The tetraphasic action of lidocaine on CNS electrical activity and behavior in cats. *Anesthesiology* 1982; **57:** 451–7.

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Anaesthesia, 1987, Volume 42, pages 1156–1161

Comparison of epidural fentanyl with sufentanil

Analgesia and side effects after a single bolus dose during elective Caesarean section

T. H. MADEJ AND L. STRUNIN

Summary

Duration of analgesia and side effects following single bolus doses of epidural fentanyl (100 μg) or sufentanil (10, 20, 30 or 50 μg) were studied in 50 patients who underwent Caesarean section under epidural anaesthesia. Fewer patients experienced pain peroperatively in the fentanyl group than in a joint group of those given sufentanil 20 or 30 μg ($p < 0.05$). The combined fentanyl and sufentanil 50 μg groups had fewer patients in pain than the sufentanil 10 μg group at 3 hours after injection ($p < 0.05$). Patients given fentanyl also had a longer pain-free interval than those who received sufentanil 10 μg ($p < 0.02$). The sufentanil 50 μg group had more patients asleep than the 10 μg group and also had more patients with pruritus than the 10 μg or 30 μg groups ($p < 0.02$). The patients given sufentanil 30 and 50 μg had more emetic sequelae than those who received sufentanil 10 and 20 μg or fentanyl 100 μg ($p < 0.05$). There was no detectable excretion of drug into breast milk and no significant respiratory depression at the time of first postoperative analgesia in the patients who received fentanyl or 30 μg or less of sufentanil.

Key words

Analgesics; fentanyl, sufentanil.
Measurement techniques; capnography, radio-immunoassay, visual analogue scale.

Women who elect to have their Caesarean section under epidural anaesthesia form a large, fairly homogeneous group for the study of postoperative pain and the effects of epidural narcotics. Morphine has been used epidurally after Caesarean section and can produce prolonged analgesia. Unfortunately, epidural morphine may also cause nausea, vomiting, pruritus, urinary retention and, most importantly, delayed respiratory depression.[1]

Various other opiates have been studied in the epidural space and those with greater lipid solubility may offer some advantages. For example, fentanyl has a fast onset of action[2] and does not cause delayed respiratory depression after a single bolus epidural dose or epidural infusion.[3,4] Administration of fentanyl 50–100 μg epidurally during Caesarean section significantly reduced intra-operative pain, prolonged postoperative analgesia and reduced postoperative analgesic requirements. In this dose range the incidence of pruritus was 40%.[5]

Sufentanil is a highly lipid soluble derivative of fentanyl, with significantly higher affinity for the opiate mu-receptor.[6] As such sufentanil would be expected to have fewer side effects. The

---

T.H. Madej, BM, BCh, FFARCS, Lecturer, L. Strunin, MD, FFARCS, FRCP(C), Professor and Head of Department, Department of Anaesthesia, Foothills Hospital at the University of Calgary, 1403 29th Street NW, Calgary, Alberta T2N 2T9, Canada.
Correspondence should be addressed to Professor L. Strunin please.

0003–2409/87/111156 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

drug may also have a longer duration of action than fentanyl when given epidurally.[7] The relative potency of sufentanil and fentanyl when given by the epidural route has not been studied.

This investigation was designed to compare the analgesic effect of a single bolus dose of epidural fentanyl with four different single bolus doses of epidural sufentanil in patients for Caesarean section. Potential side effects were sought, including respiratory depression, emetic sequelae, pruritus, somnolence and excretion into breast milk.

Methods

The study was approved by the University of Calgary Joint Ethics Committee and written informed consent was obtained from all patients. Fifty ASA class 1 or 2 patients scheduled for elective Caesarean section were enrolled in the study. A standard method was used to insert a lumbar epidural catheter and establish a sensory block to the 4th thoracic dermatome using 2% lignocaine (bicarbonate salt) with 1:200 000 adrenaline. After delivery of the baby and clamping of the cord, the patients were assigned in a random, double-blind fashion to receive an injection of sufentanil 10, 20, 30 or 50 μg or fentanyl 100 μg. All the drugs were diluted in 0.9% sodium chloride to a total volume of 10 ml and injected via the epidural catheter, through a bacterial filter, over a period of 60 seconds.

The epidural catheters were removed at the end of surgery. The patients spent one hour in the recovery room and then returned to the postpartum ward. Mothers who breast-fed their baby in the recovery room were asked to donate a sample of colostrum. Postoperative analgesia was given on request, up to 3-hourly, as morphine 0.2 mg/kg intramuscularly. Nausea or vomiting was treated with cyclizine 50 mg intramuscularly, up to 6-hourly.

Continuous monitoring of respiratory rate and end tidal carbon dioxide using a fine intranasal catheter and capnograph was started at the beginning of surgery and continued for 9 hours. Measurements were made of arterial blood pressure, pulse, level of sensory block, ability to raise both knees, pain (10-cm linear analogue score and verbal score: 0, nil; 1, mild; 2, moderate; 3, severe), somnolence (0, nil; 1, drowsy; 2, asleep), pruritus (0, nil; 1, mild; 2, moderate; 3, severe) and emesis (0, nil; 1, nausea; 2, vomiting). These were recorded 5 minutes before and immediately after the injection of epidural opiate, at 5, 10, 20, 30 and 60 minutes, then hourly for 8 hours and finally at 24 hours. The incidence of urinary retention could not be assessed since urinary catheters were retained for 24 hours. All patients were asked to give a subjective assessment of their per- and postoperative state and patients who had had a previous epidural Caesarean section were asked to compare their per- and postoperative state with their previous experience.

The concentration of opiate in colostrum was measured by radio-immunoassay. Fentanyl concentrations were measured using fentanyl (R4263) RIA kits (Janssen Life Science Products) and sufentanil concentrations were measured using a modification of the technique described by Michiels *et al.*[8] The lower limit of detection of both drugs was 0.1 ng/ml.

Data were analysed using one-way analysis of variance, Student's *t*-test, Chi-squared and Fisher's exact test. The visual analogue pain scores were interpreted as follows: 0–3.0 cm, no or mild pain; 3.1–6.6 cm, moderate pain; 6.7–10 cm, severe pain. Pain scores were analysed nonparametrically.

Results

There were 10 patients in each group with no significant differences among the groups in patient age, height or weight. The volume of local anaesthetic used, the maximum level of sensory block and the times required for recovery from

Table 1. Number of patients with pain score zero after epidural opiate.

	Fentanyl	Sufentanil			
	100 μg	10 μg	20 μg	30 μg	50 μg
Peroperatively	10	8	6*	6*	8
1 hour	10	10	10	10	10
2 hours	8	6	9	8	7
3 hours	4	0**	1	2	4
4 hours	0	0	1	2	1
5 hours	0	0	0	0	1

* Combined sufentanil 20 and 30 μg group significantly lower proportion than in fentanyl group ($p < 0.05$).

** Sufentanil 10 μg significantly lower proportion than in combined sufentanil 50 μg and fentanyl 100 μg group ($p < 0.05$).

Table 2. Mean (SEM) duration of analgesia, minutes.

	Fentanyl 100 μg	Sufentanil 10 μg	Sufentanil 20 μg	Sufentanil 30 μg	Sufentanil 50 μg
Pain score zero	131 (16)	83* (10)	107 (9)	119 (22)	137 (24)
Time to first analgesic	202 (17)	165 (15)	197 (15)	211 (19)	229 (25)

* Sufentanil 10 μg significantly less than fentanyl 100 μg ($p < 0.02$).

Table 3. Number of patients who experienced side effects after epidural opiate.

	Fentanyl 100 μg	Sufentanil 10 μg	Sufentanil 20 μg	Sufentanil 30 μg	Sufentanil 50 μg
Drowsy	3	5	7	4	3
Asleep	2	0	1	4	6*
Pruritus	4	1	5	2	9*
Nausea	2	6	3	6**	3**
Vomiting	1	0	1	3**	4**

* Sufentanil 50 μg significantly greater than sufentanil 10 μg ($p < 0.02$).

** Combined sufentanil 30 and 50 μg group significantly greater proportion than in fentanyl and combined sufentanil 10 and 20 μg group ($p < 0.05$).

sensory block and to be able to raise both knees, were similar for all groups.

In total 12 patients experienced mild or moderate pain peroperatively (Table 1) and there was no statistically significant difference in the incidence among individual groups. However, eight patients had peroperative pain in the combined group that received sufentanil 20 or 30 μg compared to none in the fentanyl group ($p < 0.05$). Thirteen patients underwent exteriorisation of the uterus and five of these experienced pain. Other causes of intra-operative pain included tubal ligation and irritation of the diaphragmatic peritoneum, despite head-up tilt. Patients with and without exteriorisation of the uterus and tubal ligation were evenly distributed through the groups. Some patients in all groups spontaneously remarked that they felt very comfortable and relaxed after the epidural opiate.

At 3 hours after epidural opiate injection eight patients in a combined fentanyl and sufentanil 50 μg group had no pain (Table 1), whereas all patients in the sufentanil 10 μg group had some pain ($p < 0.05$). The duration of complete analgesia (pain score zero) was similar for fentanyl and sufentanil 20–50 μg (Table 2). The group that received sufentanil 10 μg had a significantly shorter pain-free interval than those who received fentanyl ($p < 0.02$). The time to first postoperative analgesic did not differ significantly among the groups and all groups had a similar total morphine dose at 6, 9 and 24 hours.

Table 3 gives the numbers of patients with somnolence, pruritus and emetic sequelae in the interval after the epidural opiate and before the first postoperative analgesic. More patients were found asleep in the group that received sufentanil 50 μg compared to the 10 μg group, and more patients in the 50 μg group had pruritus than in the 10 or 30 μg groups ($p < 0.02$). If the figures for emetic sequelae are combined for sufentanil 10 with 20 μg and 30 with 50 μg, the patients given 30 μg or more of sufentanil had significantly more nausea and vomiting than those given 20 μg or less of sufentanil or fentanyl ($p < 0.05$). Those who received 30 μg or more also experienced excess vomiting compared to those who had 20 μg or less of sufentanil ($p < 0.05$).

There was no significant difference among the mean respiratory rates in the five groups at any time (range 14–20 breaths/minute). Patients given sufentanil had no significant reduction in respiratory rate during 9 hours of continuous monitoring. The group given fentanyl had a statistically, but not clinically, significant reduction in respiratory rate (lowest mean respiratory rate 15 breaths/minute (SE 0.5)) relative to control (20 breaths/minute (SE 1.0)) 120 minutes after epidural injection and 30–60 minutes after their first dose of postoperative analgesic ($p < 0.05$).

Four patients had a respiratory rate of 8 breaths/minute within 20 minutes of epidural opiate injection; three had received fentanyl and one had received sufentanil 50 μg. One patient who had received sufentanil 10 μg 8 hours previously, developed a respiratory rate of 8 breaths/minute 80 minutes after a second dose of morphine. These low respiratory rates were associated with end tidal carbon dioxide levels of 4.2–5.0 kPa.

There were statistically significant differences

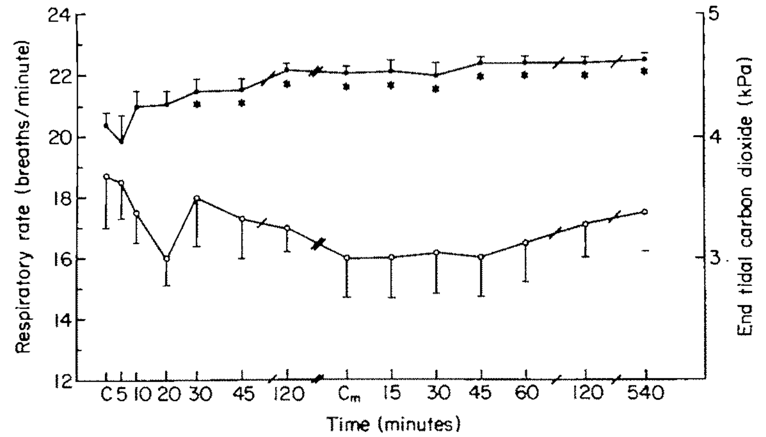


Fig. 1. Mean (SEM) values of respiratory rate (○) and end tidal carbon dioxide concentration (●) following epidural sufentanil 50 μg and intramuscular morphine 0.2 mg/kg. C, Control before sufentanil; C_m, control before morphine. * Significantly greater than control before sufentanil ($p < 0.05$).

among the mean end tidal carbon dioxide tensions of the five groups but all fell in the range 3.7–5.0 kPa. The end tidal carbon dioxide of the sufentanil 30 μg group did not increase significantly compared to control at any time. The groups given fentanyl and sufentanil 10 and 20 μg had a significant increase in end tidal carbon dioxide 15–45 minutes after the first dose of morphine ($p < 0.05$). The patients who received sufentanil 50 μg demonstrated a significant increase in end tidal carbon dioxide relative to control 30 minutes after epidural injection (Fig. 1). The end tidal carbon dioxide remained significantly elevated and there was a further significant increase 45 minutes after the first dose of morphine ($p < 0.05$).

Three patients had end tidal carbon dioxide values greater than 5.5 kPa. One had an end tidal carbon dioxide of 6.2 kPa and a respiratory rate of 12 breaths/minute 25 minutes after sufentanil 30 μg; another who received sufentanil 20 μg had end tidal carbon dioxide values up to 6.3 kPa which started 90 minutes after the first dose of morphine (15 mg intramuscularly) and continued intermittently for 6 hours, with respiratory rate remaining above 10 breaths/minute. The third received fentanyl and had end tidal carbon dioxide values up to 6.0 kPa which began 60 minutes after the first dose of morphine (15 mg intramuscularly) and continued intermittently for 4 hours, with respiratory rate remaining above 12 breaths/minute. The latter two patients did not show a further increase in end tidal carbon dioxide with subsequent doses of morphine.

Eight patients in the fentanyl group and nine patients who received sufentanil 50 μg were able to donate a sample of colostrum. These samples were obtained approximately one hour after the administration of epidural opiate. None of the samples had detectable levels of fentanyl or sufentanil.

Forty-four (88%) of all patients considered their pre- and postoperative state to be satisfactory and 83% of the 41 patients who had a previous Caesarean section considered the present experience to be better. Twenty-one patients had previous experience of epidural anaesthesia and, again, the majority (81%) considered their present experience to be better. There was no significant difference among the groups in any of these subjective assessments.

Discussion

The duration of action of lipid soluble opiates administered by the epidural route can be affected by the local anaesthetic used and by the presence of adrenaline.[9,10] In the present study the duration of pain score zero for sufentanil was similar to that found by Leicht *et al.*[11] and Donadoni *et al.*;[7] in both these studies the epidural opiate was given later, when the patient first complained of pain. Naulty *et al.*[9,10] obtained results similar to those of the present study for sufentanil and fentanyl after lignocaine but also showed a somewhat longer duration if adrenaline was added. The availability of first postoperative analgesia must be considered when its timing is examined. The nurses on the postpartum wards at Foothills Hospital encourage all patients to accept early postoperative analgesia. Tan *et al.*[12] found almost identical timing of first postoperative analgesia after epidural sufentanil using a patient-controlled system.

The incidence of somnolence after sufentanil was slightly higher than that found by Donadoni *et al.*[7] Naulty *et al.*[5] also found a lower incidence of somnolence after fentanyl. However, all the patients in the present study were easily roused and none was dissatisfied with the degree of sedation. Pruritus was also well tolerated and no patient requested treatment. The incidence of pruritus was similar to that found in earlier studies.[5,12] The high incidence of emetic sequelae was more disturbing although, again, not different from that found in other studies.[12] Very few side effects presented later than 2 hours after epidural administration, although two patients in the group that received sufentanil 50 μg and one patient who received fentanyl developed moderate pruritus at 3 hours.

Continuous respiratory monitoring detected statistically significant changes of respiratory rate and end tidal carbon dioxide among groups (fentanyl, sufentanil 10, 20 and 50 μg). The lowest respiratory rates were not associated with high end tidal carbon dioxide levels. There were no respiratory rates below 8 breaths/minute and no episodes of apnoea. This contrasts with the high incidence of respiratory abnormalities found by Whiting *et al.*[13] after epidural sufentanil 30–75 μg. However, this probably reflects a difference in patient population; Whiting's patients were older and would have had reduced ventilatory capacity after a thoracotomy and general anaesthetic. These factors have been shown to increase the risk of respiratory depression after epidural opiates.[14] Before the first dose of morphine postoperatively only the end tidal carbon dioxide of the sufentanil 50 μg group differed significantly from control. Unlike epidural morphine (3.5–7 mg), the respiratory depression due to epidural fentanyl up to 100 μg and sufentanil up to 30 μg does not appear to outlast the analgesic effect.[15] The increased end tidal carbon dioxide values and reduced respiratory rates recorded on the ward after postoperative analgesia were not greater than seen after intramuscular morphine alone.[16]

One hour after epidural administration neither fentanyl nor sufentanil was detectable in colostrum. At Foothills Hospital this is the time when the majority of mothers first breast-feed their baby. This practice can continue in conjunction with the use of epidural fentanyl or sufentanil and the baby will not receive a significant dose of either of these opiates.

In conclusion, both sufentanil and fentanyl have a rapid onset and short duration of action when administered epidurally. Sufentanil 50 μg had an unacceptably high incidence of side effects. Epidurally sufentanil 20–30 μg seemed to be equivalent to fentanyl 50–100 μg, which implies that the potency ratio for epidural administration is less than after intravenous administration.[17] Sufentanil offers no advantage over fentanyl for single bolus epidural administration in terms of increased duration or reduced side effects. Both are useful to treat peroperative pain or agitation and give early postoperative analgesia. In ASA grade 1 or 2 obstetric patients a single bolus dose of epidural fentanyl 100 μg or sufentanil up to 30 μg may be supplemented with intramuscular opiates on patient request with little risk of significant residual respiratory depression from the epidural opiate.

Acknowledgments

The authors thank Mrs M. A. Sabourin for carrying out the radio-immunoassay and Janssen Pharmaceuticals Inc. for supplying the radioimmunoassay kits. They also acknowledge gratefully the assistance of the nursing staff of the Labour and Delivery Suite at Foothills Hospital and Mrs A. Cuppage, Anaesthetic Department Research Nurse.

References

1. Leicht CH, Hughes SC, Daily PA, Schnider SM, Rosen MA. Epidural morphine sulfate for analgesia after cesarean section: a prospective report of 1000 patients. *Anesthesiology* 1986; **65:** A366.
2. Welchew EA. The optimum concentration for epidural fentanyl. A randomised, double-blind comparison with and without 1:200 000 adrenaline. *Anaesthesia* 1983; **38:** 1037–41.
3. Rutter DV, Skewes DG, Morgan M. Extradural opioids for postoperative analgesia. A double-blind comparison of pethidine, fentanyl and morphine. *British Journal of Anaesthesia* 1981; **53:** 915–20.

4. Ahuja BR, Strunin L. Respiratory effects of epidural fentanyl. *Anaesthesia* 1985; **40:** 949–55.
5. Naulty JS, Datta S, Ostheimer GW, Johnson MD, Burger GA. Epidural fentanyl for post-cesarean delivery pain management. *Anesthesiology* 1985; **63:** 694–8.
6. Leysen JE, Gommeren W, Niemegeers CJE. [3H]Sufentanil, a superior ligand for μ-opiate receptors: binding properties and regional distribution in rat brain and spinal cord. *European Journal of Pharmacology* 1983; **87:** 209–25.
7. Donadoni R, Rolly G, Noorduin H, Van den Busche G. Epidural sufentanil for postoperative pain relief. *Anaesthesia* 1985; **40:** 634–8.
8. Michiels M, Hendricks R, Heykants J. Radioimmunoassay of the new opiate analgesics alfentanil and sufentanil. Preliminary pharmacokinetic profile in man. *Journal of Pharmacy and Pharmacology* 1983; **35:** 86–93.
9. Naulty JS, Hertwig L, Hunt CO, Hartwell B, Datta S, Ostheimer GW, Covino BG. Duration of analgesia of epidural fentanyl following cesarean delivery—effects of local anesthetic drug selection. *Anesthesiology* 1986; **65:** A180.
10. Naulty JS, Sevarino FB, Lema MJ, Hunt CO, Datta S, Ostheimer GW. Epidural sufentanil for postcesarean delivery pain management. *Anesthesiology* 1986; **65:** A396.
11. Leicht CH, Rosen MA, Dailey PA, Hughes SC, Schnider SM, Baker BW, Cheek DB, O'Connor DE. Evaluation and comparison of epidural sufentanil citrate and morphine sulfate for analgesia after cesarean section. *Anesthesiology* 1986; **65:** A365.
12. Tan S, White PF, Cohen SE. Sufentanil for post-cesarean analgesia: epidural vs. intravenous administration. *Anesthesiology* 1986; **65:** A398.
13. Whiting WC, Sandler AN, Lau LC, Chovaz PM. Analgesic and respiratory effects of epidural sufentanil in post-thoracotomy patients. *Anesthesiology* 1986; **65:** A176.
14. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *British Journal of Anaesthesia* 1982; **54:** 479–86.
15. Knill RL, Clement JL, Thompson WR. Epidural morphine causes delayed and prolonged ventilatory depression. *Canadian Anaesthetists' Society Journal* 1981; **28:** 537–43.
16. Smith TC, Stephen GW, Zeiger L, Wollman H. Effects of premedicant drugs on respiration and gas exchange in Man. *Anesthesiology* 1967; **28:** 883–90.
17. Rosen CE. Sufentanil citrate: a new opioid analgesic for use in anaesthesia. *Pharmacotherapy* 1984; **4:** 11–18.

Anaesthesia, 1987, Volume 42, pages 1162–1170

High frequency ventilation and afferent vagal activity

A. W. HARROP-GRIFFITHS, M. K. CHAKRABARTI
AND J. G. WHITWAM

Summary

Recordings were made from pulmonary afferent fibres in the vagus nerves of anaesthetised dogs during conventional and high frequency ventilation. In single and multiple fibre preparations, the mean spike counts per minute at 14 breaths/minute were in the ranges 36.9–155.3 and 755–1921, respectively. These counts decreased by up to 61 and 44% respectively at 100 breaths/minute, and by 27–89% and 22–51% at 200 breaths/minute. At this frequency there was a further decrease of between 19 and 65% when the positive end expiratory pressure was removed. The findings of this study are intuitively acceptable, since pulmonary stretch receptor activity is proportional to tidal volume, and are in keeping with the clinical impression that high frequency ventilation per se does not eliminate respiratory drive.

Key words

Measurement techniques; vagus nerve activity.
Ventilation; high frequency.

Ventilation with low tidal volumes at high frequencies has been recommended for patients with respiratory distress syndromes.[1–3] Jonzon[4] showed that in cats, as the ventilation frequency increased towards 100 breaths/minute, there was an increase in total afferent activity in the vagus nerve. He observed the development of positive end expiratory pressure during high frequency ventilation but did not correlate this with the observed respiratory-phased afferent and efferent activity in the vagus and phrenic nerves, respectively.

More recently, Man *et al.*[5] have shown that during high frequency oscillatory ventilation in dogs at 25 Hz, there was an increase in afferent vagal activity from the lungs. These authors also related this to the ventilation frequency but they failed to separate the effect of high frequency oscillatory ventilation from that due to the development of positive end expiratory pressure.

The present study was undertaken to re-examine the effect of high frequency ventilation on afferent vagal activity and to delineate the contribution of positive end expiratory pressure to the observed changes.

Methods

Observations were made on seven mongrel dogs in which anaesthesia was induced with a bolus dose of methohexitone 10–12 mg/kg intravenously, and maintained with a 1% solution of

---

A.W. Harrop-Griffiths, MB, BS, FFARCS, Registrar, M.K. Chakrabarti, BSc, MPhil, Senior Chief Technician, J.G. Whitwam, MB, ChB, PhD, FRCP, FFARCS, Professor of Anaesthesia, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road, London W12 0HS.

Correspondence should be addressed to Professor J.G. Whitwam please.

0003–2409/87/111162 + 09 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

alpha-chloralose administered initially as a bolus dose of 3 ml/kg and later as a continuous intravenous infusion of 1–2 ml/kg/hour. The dogs' lungs were artificially ventilated via a tracheal tube. Neuromuscular blockade was produced with suxamethonium 1–2 ml/kg/hour intravenously. Catheters for pressure monitoring were inserted into the inferior vena cava via a femoral vein, and into a femoral artery.

Either the right or the left vagus nerve was exposed in the neck and a section was desheathed. Single fascicles were dissected from the desheathed portion of the nerve and were cut proximally, teased down to a few fibres, mounted on bipolar silver electrodes and immersed in mineral oil. The signal was amplified (Tektronix 122) and only fibres that showed inspiratory phased activity at a control ventilation frequency of 14 breaths/minute were studied. Single and multiple fibre recordings were obtained by passing the signal through a spike processor with an adjustable gating circuit (Digitimer 130). The action potentials from either single or multifibre preparations, referred to as unprocessed data, were used to trigger a pulse generator, the output of which is referred to as processed data. Both the unprocessed and processed data were displayed on an oscilloscope (Tektronix 565) and were recorded, along with intravascular and intratracheal pressures, on an ultraviolet recorder (SE Laboratories, Type 2112). The processed spike count breath by breath was counted for one-minute intervals and was recorded with a suitably calibrated Devices MX2 pen recorder. The figures in the spike count tables represent the mean and standard deviation obtained from at least five one-minute recording periods.

The arterial oxygen ($P\text{aO}_2$), carbon dioxide ($P\text{aCO}_2$) tensions and pH were maintained in the ranges 11.4–14 kPa, 5.1–5.6 kPa and 7.25–7.40, respectively, and were kept within 5% of their baseline values throughout any experimental period except during periods of apnoeic oxygenation, when $P\text{aO}_2$ was greater than 55 kPa and $P\text{aCO}_2$ increased to between 7.5 and 9.5 kPa. The core temperature, measured by an oesophageal thermistor, was maintained in the range 37–39°C.

The conduction velocities, spike durations and stimulus thresholds of the single fibres from which recordings had been made, were measured. A portion of the vagus nerve 10–12 cm distal to the recording site was dissected clear of the tissues. The external sheath was removed to expose the fascicles in the nerve. During short periods of apnoeic oxygenation, when spontaneous spike activity was absent, single electrical stimuli were applied to the nerve at this point and the evoked action potential was recorded at the original site which had been left undisturbed. The stimulus threshold for each fibre was determined by progressively increasing the intensity of the electrical stimulus (duration 0.05 milliseconds, frequency 1 Hz). The electrical stimulus and the evoked action potential were displayed on an oscilloscope so that the spike duration and conduction time could be determined. Measurement of the nerve length between the stimulating cathode, placed relative to the anode, in the direction of the conducted action potential, and the proximal recording electrode, i.e. the one nearest the stimulating cathode, allowed the calculation of the conduction velocity of each single fibre from which recordings had been made.

The preparations were ventilated with a new, valveless ventilator,[6,7] the circuit of which is illustrated in Fig. 1. It allows, when required, the application of either positive or negative end expiratory pressure and, hence, the removal of positive end expiratory pressure generated during high frequency ventilation (Fig. 2). An inspiration to expiration ratio of 1:2 was used throughout (Fig. 3).

After a period of stabilisation at a ventilation frequency of 14 breaths/minute, recordings of afferent vagal activity were made at frequencies of 14, 100 and 200 breaths/minute, followed by a return to control frequency. The effect of the application of 0.5 and 1.0 kPa positive end expiratory pressure was examined at frequencies of 14, 100 and 200 breaths/minute, and also during apnoeic oxygenation in the absence of respiratory movement. The effect of the application of negative end expiratory pressure to the point at which there was zero end expiratory pressure, was observed at a frequency of 200 breaths/minute.

Statistical analysis was performed using analysis of variance and paired Student's *t*-tests where relevant. A probability of less than 0.05 was accepted as significant.

Results

The conduction velocities, spike durations and

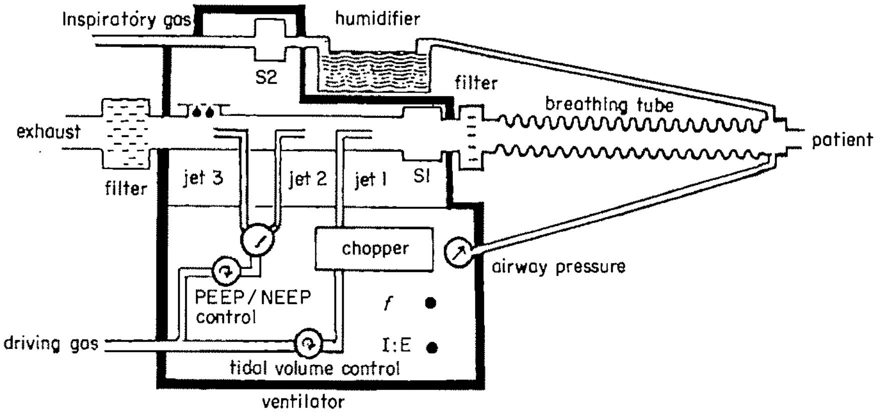


Fig. 1. In this new ventilator a driving jet (jet 1) is placed in the wide-bore breathing limb of a T-piece and the respiratory fresh gas is supplied near the mouth at a flow rate of at least normal minute volume (i.e. approximately 100 ml/kg) during controlled ventilation. The design is such that the jet driving gas does not take part in gas exchange, because the breathing tube volume between the fresh gas entry and the driving jet is greater than one tidal volume. The tidal volume is set by adjusting the driving pressure to jet 1 which works as a pneumatic piston. The ventilation frequency and inspiration to expiration ratio are controlled by an electronic pulse generator that drives a solenoid valve. The expired tidal volume is measured by the use of two flow sensors, one of which measures the total expired volume and the other, the fresh gas volume for the expiratory time taken from the jet pulse generator. The difference between these two volumes is obtained electronically and displayed as the V_T. Jets 2 and 3 provide positive and negative end expiratory pressure, respectively.

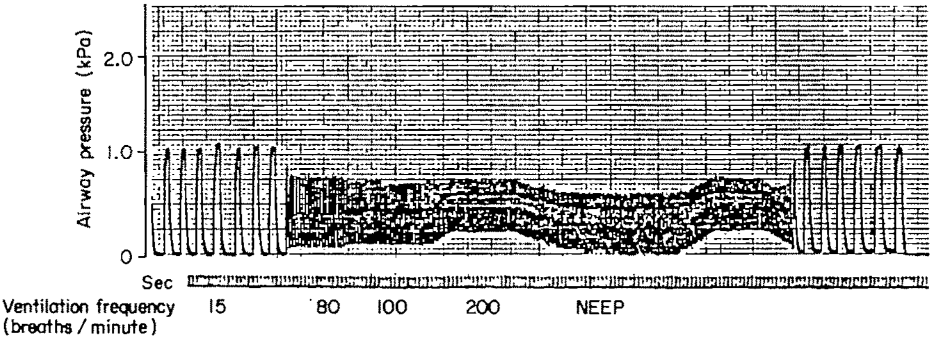


Fig. 2. Airway pressure (P_{AW}) at different ventilation frequencies. Time marker in seconds. NEEP, application of negative end expiratory pressure jet to reduce end expiratory pressure to zero.

thresholds for stimulation (with a stimulus duration of 0.05 milliseconds) were 15–60 metres/second, 0.7–1.2 milliseconds and 1.5–3.0 V, respectively. This implies that the recordings were all made from myelinated fibres in groups II and III, since the values for conduction velocities and threshold stimulus intensities for unmyelinated fibres would be smaller and greater respectively by several orders of magnitude.[8]

The airway pressures recorded at different ventilation frequencies are illustrated in Fig. 2. The positive end expiratory pressures developed at 100 and 200 breaths/minute were approximately 0.1 and 0.25 kPa, respectively, and these could be returned to zero using the negative end expiratory pressure jet of the ventilator,[6] labelled jet 3 in Fig. 1.

The waveform of the airway pressure is illustrated in Fig. 3 together with the action potentials (AVA upper trace) from a multifibre

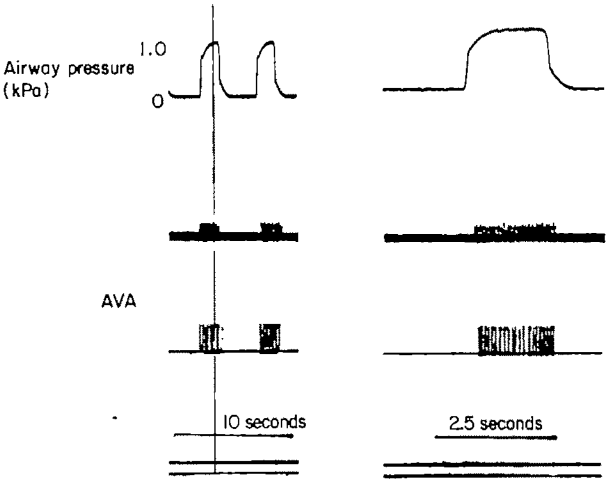


Fig. 3. Airway pressure (P_{AW}) and afferent vagal activity (AVA) in a multifibre preparation. AVA: upper trace, unprocessed recording; lower trace, output from a spike generator triggered by the action potentials from three fibres. Ventilation rate 14 breaths/minute; inspiration to expiration ratio 1:2.

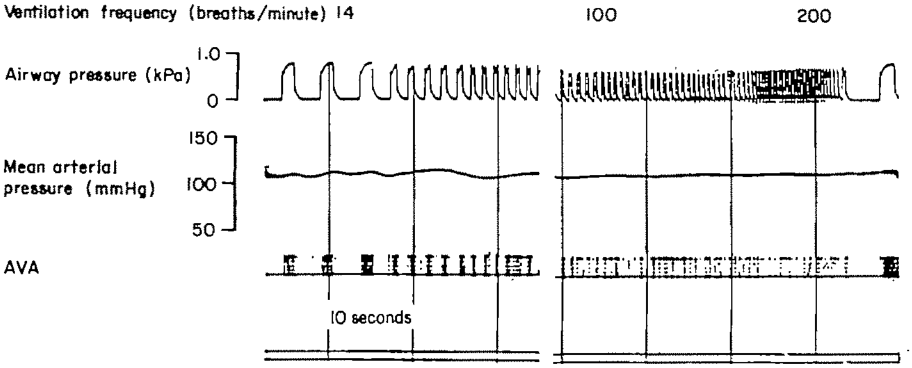


Fig. 4. Effect of different ventilation frequencies on mean arterial pressure and processed afferent vagal activity in a multifibre preparation. AVA, afferent vagal activity (processed). Marker lines at 10-second intervals.

preparation during ventilation at 14 breaths/minute. The processed data from a recording that contains action potentials from three fibres, are shown in the lower trace. They had different spike heights but each produced the same output from the pulse generator.

Effect of increasing the ventilation frequency

Figure 4 shows the airway pressure, mean arterial pressure and processed afferent vagal activity recorded from a multiple fibre preparation during an increase in ventilation frequency from 14 to 200 breaths/minute, subsequently returning to 14 breaths/minute.

In Table 1 it can be seen that the mean spike counts in five multifibre recordings, each from a different preparation, were in the range 755–1921 spikes/minute. When the ventilation frequency was increased from 14 to 100 breaths/minute, there was a decrease in the mean total spike counts in the range of 92.1–837.8/minute. Expressing the spike count decreases as a percentage fall from control values, the minimum decrease seen was 12% and the maximum was 44%. When the ventilation frequency was increased

Table 1. Multiple fibre preparations: mean (SD) spike counts/minute. Each figure is the mean value from five one-minute counts during an 8–10-minute period, after stabilisation and adjustment of blood gas tensions to near control values after each change in ventilation frequency.

	Respiratory frequency, breaths/minute			
	14	100	200	14
Preparation number	A	B	C	D
1	755.0 (45.6) BC*	662.9 (47.1) ACD	565.0 (46.6) ABD	768.0 (62.6) BC
2	991.2 (64.8) BC	710.0 (33.2) AD	776.0 (74.2) AD	910.0 (32.6) BC
3	1340.0 (69.2) BC	790.0 (34.2) ACD	656.0 (32.0) ABD	1274.0 (105.6) BC
4	1446.6 (48.6) BC	933.4 (34.0) ACD	833.4 (9.4) ABD	1371.4 (82.0) BC
5	1921.0 (406.3) BC	1083.2 (179.2) AD	1134.3 (163.4) AD	1804.7 (217.7) BC

The letters below the numbers in the table indicate the columns compared and imply that the value is significantly different from those in columns indicated by these letters ($p < 0.05$).

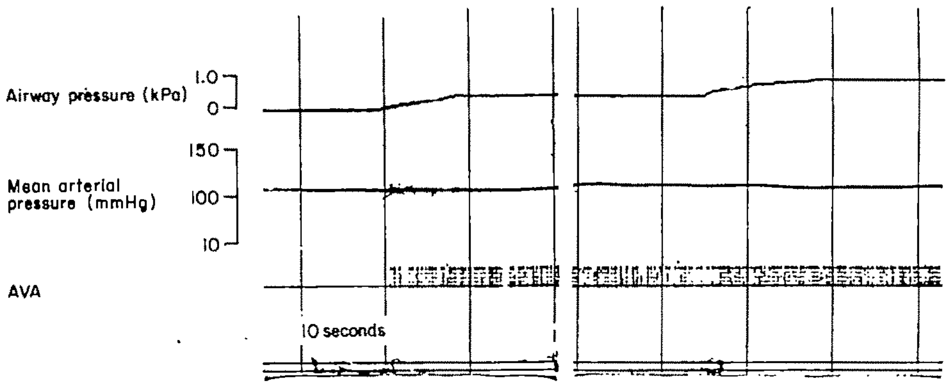


Fig. 5. Effect of positive end expiratory pressure on processed spike activity during apnoeic oxygenation. AVA, afferent vagal activity (processed). Marker lines at 10-second intervals.

to 200 breaths/minute the range of mean total spike count decrease was 190–786.7 spikes/minute, and the range of percentage decrease from control was 22–51%. In five single fibre recordings (Table 2), the mean spike counts at control ventilation frequency were in the range 36.9–155.3 counts/minute. At 100 breaths/minute there was a decrease in the mean spike count of between 15.6 and 90.2 spikes/minute. At 200 breaths/minute, the decrease was in the range 18.7–127.5 spikes/minute. The ranges of percentage decrease from control values were 19–61% at 100 breaths/minute and 27–89% at 200 breaths/minute for the single fibre preparations.

Effect of positive end expiratory pressure

Figure 5 shows the airway pressure, mean arterial pressure and processed afferent vagal activity recorded from a multiple fibre preparation during an increase in positive end expiratory pressure from 0 to 1.0 kPa during apnoeic oxygenation. Table 3 shows the effect of increasing the positive end expiratory pressure from 0 through 0.5 kPa and up to 1.0 kPa on the mean spike count/minute for two single, and two multiple fibre preparations, during apnoeic oxygenation, and at ventilation frequencies of 14, 100 and 200 breaths/minute. Mean spike counts/minute increased significantly with each increase of positive end expiratory pressure in all fibres at all ventilation frequencies. During apnoeic oxygenation in a single fibre preparation the mean spike count/minute increased to 80 and 213.3 at positive end expiratory pressures of 0.5 kPa and 1.0 kPa, respectively (Table 3). In three other

Table 2. Single fibre preparations: mean (SD) spike counts/minute. Each figure is the mean value from five one-minute counts during an 8–10-minute period, after stabilisation and adjustment of blood gas tensions to near control values after each change in ventilation frequency.

	Respiratory frequency, breaths/minute			
Preparation number	14 A	100 B	200 C	14 D
1	36.9 (5.9) BC	19.1 (6.5) ACD	3.9 (2.6) ABD	35.1 (7.7) BC
2	70.0 (7.1) C	54.4 (10.6)	51.3 (7.4) AD	68.0 (10.2) C
3	122.1 (17.9) BC	70.7 (7.5) AD	86.0 (2.0) AD	112.0 (4.0) BC
4	148.8 (32.3) BC	58.6 (10.0) ACD	21.3 (3.8) ABD	126.4 (17.4) BC
5	155.3 (8.1) BC	126.4 (5.4) ACD	94.0 (2.0) ABD	147.2 (8.2) BC

The letters below the numbers in the table indicate the columns compared and imply that the value is significantly different from those in columns indicated by these letters ($p < 0.05$).

Table 3. The effect of positive end expiratory pressure on afferent vagal activity: mean (SD) spike counts/minute. *Preparation 1*: single fibre recording during apnoeic oxygenation. *Preparations 2 and 4*: two separate multiple fibre recordings at ventilation frequencies of 14 and 200 breaths/minute, respectively. *Preparation 3*: single fibre recording at ventilation frequency of 100 breaths/minute.

Preparation number	Fibre	Respiratory frequency, breaths/minute	Positive end expiratory pressure, kPa			
			0 A	0.5 B	1.0 C	0 D
1	Single	0	0 (0) BC	80.0 (3.1) ACD	213.3 (37.7) ABD	0 (0) BC
2	Multiple	14	642.9 (165.8) C	800.0 (149.7) CD	1740.0 (566.0) ABD	516.0 (111.3) BC
3	Single	100	544.4 (10.6) BC	74.7 (5.0) ACD	124.0 (19.4) ABD	46.0 (1.2) BC
4	Multiple	200	613.4 (90.0) BC	980.0 (71.2) ACD	1720.0 (130.6) ABD	710.0 (57.6) BC

The positive end expiratory pressure was adjusted either upwards or downwards by the positive end expiratory pressure and negative end expiratory pressure jets, respectively, on the ventilator to the absolute values shown in this table. The letters below the numbers in the table indicate the columns compared and imply that the value is significantly different from those in columns indicated by these letters ($p < 0.05$).

Table 4. The effect of the removal of positive end expiratory pressure on afferent vagal activity: mean (SD) spike counts/minute. *Columns A and B*: recordings from two single and two multiple fibre preparations at ventilation frequencies of 14 and 200 breaths/minute. *Column C*: recordings after reduction of the positive end expiratory pressure to zero (0 PEEP) by the use of the negative end expiratory pressure jet (see Fig. 1). *Column D*: recordings after return of ventilation frequency to 14 breaths/minute.

		Respiratory frequency, breaths/minute			
Preparation number	Fibre	14 A	200 B	200 (0 PEEP) C	14 D
1	Single	40.1 (13.3) BC	23.0 (5.9) ACD	8.0 (4.9) ABD	34.4 (6.0) BC
2	Single	70.0 (7.1) BC	51.3 (7.4) ACD	32.0 (10.1) ABD	64.4 (13.8) BC
3	Multiple	1045.0 (31.2) BC	550.0 (17.6) ACD	445.0 (21.8) ABD	1180.0 (85.4) BC
4	Multiple	1446.6 (48.6) BC	833.4 (9.4) ACD	653.4 (39.8) ABD	1371.4 (82.0) BC

The letters below the numbers in the table indicate the columns compared and imply that the value is significantly different from those in columns indicated by these letters ($p < 0.05$).

preparations, ventilated at 14, 100 and 200 breaths/minute, there was a two- to threefold increase in mean spike count when the positive end expiratory pressure was adjusted to 1.0 kPa.

Effect of the elimination of positive end expiratory pressure

An example of airway pressures recorded during an increase in ventilation frequency from 14, through 100, to 200 breaths/minute, the development of positive end expiratory pressure at high ventilation frequencies, and the use of the negative end expiratory pressure jet to reduce the positive end expiratory pressure to zero, is shown in Fig. 2. This ventilatory profile was used in this part of the study.

The results can be seen in Table 4 for two single, and two multiple fibre preparations. By 200 breaths/minute the mean spike counts/minute decreased between 17.1 and 613.2 spikes/minute and from 27–47% in different preparations compared with the control values at 14 breaths/minute. When the end expiratory pressure was returned to zero, at 200 breaths/minute there was a further decrease in mean spike count of between 15 and 180 spikes/minute and between 19–65% in different preparations.

Discussion

This study shows that, during high frequency ventilation, there was a decrease in the total number of respiratory-phased action potentials that travel in afferent fibres in the vagus nerves, and that the removal of the positive end expiratory pressure generated during the application of high frequency ventilation, further enhanced this effect.

Jonzon[4] recorded activity in the whole vagus nerve during high frequency ventilation in cats. He commented on an increase in 'basal discharge' but did not refer to the decrease in the maximum discharge peaks synchronous with inspiration when ventilation frequency increased. He did not correlate the changes observed with the positive end expiratory pressure developed at higher ventilation frequencies. Hence it could be argued that his findings can be interpreted as in broad agreement with the present study. Man *et al.*[5] ventilated the lungs of dogs conventionally at 18 breaths/minute and then with high frequency oscillation at 1500 breaths/minute. However, they took no account of the effect of the positive end expiratory pressure developed during high frequency oscillation, and an analysis of their data, presented in the short appendix to this paper, reveals results similar to those reported here.

The recordings in the present study showed a respiratory modulation so that activity occurred during inflation of the lungs. During the application of a sustained positive airway pressure in the absence of ventilation during apnoeic oxygenation, the recordings showed either no adaptation or evidence of only very slow adaptation during periods up to 5 minutes. Hence the pulmonary stretch receptors responsible for the recorded activity would be classified as type I.[9] The conduction velocities and spike duration of the fibres recorded in the present study would be compatible with this view.

The literature concerning the action of vagus nerve activity on respiratory control is so extensive that this brief discussion cannot hope to do justice to previous work. For example, in 1933 Adrian[10] demonstrated afferent activity in the vagus nerve with both respiratory and cardiac modulations. Miserocchi and Milic-Emili[11] showed that hypercapnia affects respiratory frequency by increasing the sensitivity of the respiratory centres to a given phasic vagal input, while Richardson and Widdicombe[12] showed that vagotomy depresses and flattens the upper part of carbon dioxide response curves. For a recent comprehensive review of the subject, the reader is referred to the work of Long and Duffin.[13]

Cessation of spontaneous respiratory effort is often seen in experimental and clinical subjects during high frequency ventilation. Thompson *et al.*[14] showed that in dogs, this apnoea was reversed by vagotomy, which implies that increased afferent vagal activity is responsible for the reciprocal decrease in phrenic nerve activity during high frequency ventilation.[4] However, that this increased afferent vagal activity is due primarily to the positive end expiratory pressure generated in association with an increase in lung volume[15] during high frequency ventilation, was suggested by the work of Whitwam *et al.*[16] These authors demonstrated that in dogs, decreased phrenic nerve activity observed during high frequency ventilation in the presence of positive end expiratory pressure, returned to control values when the positive end expiratory pressure was eliminated. They showed that, in this situation, phrenic nerve activity was related more to blood gas tensions than to the effect of high frequency ventilation *per se*.

Some of the action potentials could be recorded simultaneously in processed data from multifibre recordings so that, for example, two or more would be superimposed and would generate only one signal which in turn would trigger only one signal from the pulse generator. This phenomenon tended to occur at the high firing frequencies and, thus, the results reported here would tend to underestimate the decrease in the number of action potentials recorded per minute when moving from lower to higher ventilation frequencies. Moreover, the findings in single fibre preparations, where this problem does not arise, show the same trend as the multifibre recordings.

The findings reported here are intuitively acceptable, since a small tidal volume would be expected to provide only a small stimulus to the pulmonary stretch receptors compared with the larger volumes associated with conventional ventilation. Thus the total number of action potentials per breath would be expected to be reduced and, even though the number of breaths/minute increased, the total spike count/minute was still less than control values at the lower frequencies of ventilation. In spite of the more rapid stimulus to the receptors at higher ventilation frequencies, there was never any evidence of 'overshoot' of the rate of firing of the action potentials, which can be seen with some types of stretch receptors.[17]

In conclusion, the results of this and previous studies mentioned above, suggest that the common experimental and clinical observation of reduced central respiratory drive during high frequency ventilation, is due principally to the development of a significant positive end expiratory pressure and an improvement in blood gas status, rather than to the effect of high frequency ventilation *per se*.

Appendix

Man *et al.*[5] described recordings from 13 vagal nerve units in studies on 14 dogs. They recorded afferent vagal activity during intermittent positive pressure ventilation at a frequency of 18 breaths/minute and during high frequency oscillation at 25 Hz. The latter generated a positive end expiratory pressure of 8 cm H_2O, so they also recorded activity with airway occlusion at a standing pressure of 8 cm H_2O in the absence of ventilation. Their recorded figures are given below:

	Mean (SD) impulses/minute
18 breaths/minute (zero positive end expiratory pressure)	745 (619)
High frequency oscillation (8 cm H_2O positive end expiratory pressure)	1840 (1189)
Airway occlusion (standing pressure 8 cm H_2O)	1334 (1096)

The mean afferent vagal activity attributable to high frequency oscillation alone, is

$$1840 - 1334 = 506 \text{ impulses/minute}$$

This constitutes a decrease in mean afferent vagal activity from 745 impulses/minute at 18 breaths/minute to 506 impulses/minute during high frequency oscillation. This decrease, of 32%, is in broad agreement with the figures in the present study, although the above authors did not place this interpretation upon their results.

Acknowledgment

This work was entirely supported by a grant from the Association of Anaesthetists of Great Britain and Ireland.

References

1. SJOSTRAND U. High-frequency positive-pressure ventilation (HFPPV): a review. *Critical Care Medicine* 1980; **8:** 345–64.
2. BUTLER WJ, BOHN DJ, BRYAN AC, FROESE AB. Ventilation by high-frequency oscillation in humans. *Anesthesia and Analgesia* 1980; **59:** 577–84.
3. CARLON GC, KAHN RC, HOWLAND WS, RAY C, TURNBULL AD. Clinical experience with high frequency jet ventilation. *Critical Care Medicine* 1981; **9:** 1–6.
4. JONZON A. Phrenic and vagal nerve activities during spontaneous respiration and positive-pressure ventilation. *Acta Anaesthesiologica Scandinavica* 1977; **64** (Suppl): 29–35.
5. MAN GCW, MAN SFP, KAPPAGODA CT. Effects of high-frequency oscillatory ventilation on vagal and phrenic nerve activities. *Journal of Applied Physiology* 1983; **54:** 502–7.
6. CHAKRABARTI MK, WHITWAM JG. A new valveless all-purpose ventilator. Description and laboratory evaluation. *British Journal of Anaesthesia* 1983; **55:** 1005–15.
7. WHITWAM JG, CHAKRABARTI MK, KONARZEWSKI

WH, Askitopoulou H. A new valveless all-purpose ventilator. Clinical evaluation. *British Journal of Anaesthesia* 1983; **55:** 1017–23.

8. Whitwam JG, Kidd C, Fussey IV. Responses in sympathetic nerves of the dog evoked by stimulation of somatic nerves. *Brain Research* 1979; **165:** 219–33.
9. Miserocchi G, Sant Ambrogio G. Responses of pulmonary stretch receptors to static pressure inflations. *Respiration Physiology* 1974; **21:** 77–85.
10. Adrian ED. Afferent impulses in the vagus and their effect on respiration. *Journal of Physiology* 1933; **79:** 332–58.
11. Miserocchi G, Milic-Emili J. Contribution of hypercapnic stimuli and of vagal afferents to the timing of breathing in anesthetized cats. *Respiration Physiology* 1975; **25:** 71–88.
12. Richardson PS, Widdicombe JG. The role of the vagus nerves in the ventilatory responses to hypercapnia and hypoxia in anaesthetized and unanaesthetized rabbits. *Respiration Physiology* 1969; **7:** 122–35.
13. Long S, Duffin J. The neuronal determinants of respiratory rhythm. *Progress in Neurobiology* 1986; **27:** 101–82.
14. Thompson WK, Marchak BE, Bryan AC, Froses AB. Vagotomy reverses apnea induced by high-frequency oscillatory ventilation. *Journal of Applied Physiology* 1981; **51:** 1484–7.
15. Saari AF, Rossing TH, Solway J, Drazen JM. Lung inflation during high-frequency ventilation. *American Review of Respiratory Disease* 1984; **129:** 333–6.
16. Whitwam JG, Chakrabarti MK, Askitopoulou H, Sapsed S. Effect of frequency of ventilation, positive end-expiratory pressure, Pa_{O_2}, and Pa_{CO_2} on phrenic nerve activity. A study using a new valveless all-purpose ventilator. *British Journal of Anaesthesia* 1984; **56:** 187–93.
17. Eyzaguirre C, Fidone SJ. Sensory systems. In: Eyzaguirre C, Fidone SJ, eds. *Physiology of the nervous system*, 2nd edn. Chicago: Year Book Medical Publishers, 1975: 61–162.

Anaesthesia, 1987, Volume 42, pages 1171–1175

Epidural sufentanil versus intramuscular buprenorphine for postoperative analgesia

A double-blind comparative trial

R. DONADONI AND G. ROLLY

Summary

Epidural sufentanil 50 μg was compared with intramuscular buprenorphine 0.3 mg for postoperative pain relief. Patients were assigned randomly to one of two treatment groups and received both an intramuscular and epidural injection, one of which was a placebo. Onset of pain relief was faster and quality of analgesia superior during the first 2 hours in the patients who received epidural sufentanil but the duration of analgesia was longer in the buprenorphine group. Cardiovascular variables remained stable in all patients and no respiratory depression was observed. Side effects were more frequent following buprenorphine.

Key words

Anaesthetic techniques; regional, epidural.
Analgesics, narcotic; sufentanil, buprenorphine.

Early reports on the use of sufentanil via the epidural route for postoperative pain relief showed that a dose of 50 μg produced effective pain relief with rapid onset and a duration of approximately 6–8 hours; moderate sedation was the main side effect.[1–3] Compared to epidural morphine, sufentanil provided pain relief of shorter duration but of a faster onset and better quality during the first hours.[3] The aim of this trial was to compare the efficacy and safety of epidural sufentanil with a routinely used technique of postoperative pain relief, namely, intramuscular buprenorphine. This was selected because of its reportedly similar properties with regard to quality and duration of analgesia.[4,5]

Methods

Sixty patients (ASA grade 1 or 2) scheduled for orthopaedic surgery under epidural anaesthesia with lignocaine 2% plus adrenaline 1:200 000 were included in the trial. The study was approved by the ethics committee of the Academic Hospital and informed consent was obtained from all patients.

The epidural catheter was introduced at the start of anaesthesia and was left in place throughout. The tip of the catheter was aimed at the T_{12}–L_1 level. Two double-blind ampoules were prepared for each patient which contained either 1 ml buprenorphine 0.3 mg for intramuscular use and 10 ml saline 0.9% for epidural use, or 1 ml saline 0.9% and 10 ml sufentanil 50 μg in saline 0.9% for intramuscular and epidural use, respectively.

As soon as uncomfortable pain occurred in the early postoperative period, the patient was randomly assigned to one of the two treatment

---

R. Donadoni, MD, Staff Anaesthetist, G. Rolly, MD, PhD, Professor in Anaesthesia, Head of Department of Anaesthesia, State University of Ghent, Academic Hospital, De Pintelaan 185, B-9000 Ghent, Belgium.

0003–2409/87/111171 + 05 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

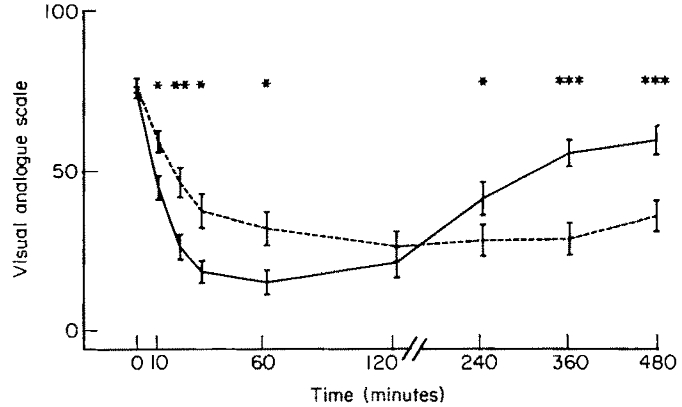


Fig. 1. Evolution of pain relief during observation period. ——, 50 μg epidural sufentanil; – – –, 0.3 mg intramuscular buprenorphine. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

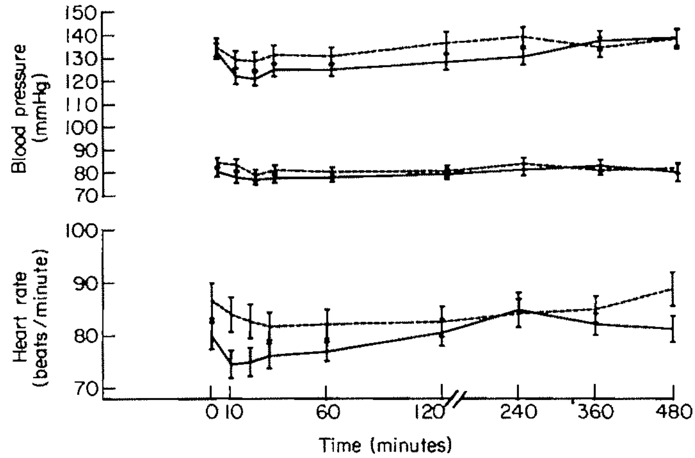


Fig. 2. Changes in blood pressure and heart rate during observation period. ——, 50 μg epidural sufentanil; – – –, 0.3 mg intramuscular buprenorphine.

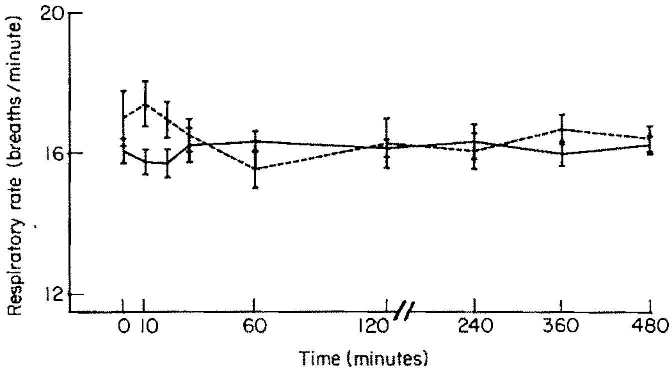


Fig. 3. Changes in respiratory rate during observation period. ——, 50 μg epidural sufentanil; – – –, 0.3 mg intramuscular buprenorphine.

groups and received both an intramuscular and epidural injection; one was the placebo. Thereafter the epidural catheter was withdrawn. Patients were asked to score the severity of pain on a 10-cm visual analogue scale before and 10, 20, 30, 60, 120, 360 and 480 minutes following administration of the double-blind medication. At the same time intervals, respiratory rate, arterial blood pressure and heart rate were recorded. Blood gases were determined only if the respiratory rate was below 10 breaths/minute.

Onset of analgesia was defined as the time (minutes after injection) when the patient experienced pain relief, and duration of analgesia as the time interval between injection and request for further analgesia. The observer also evaluated the quality of pain relief using a four-point scoring system: excellent, good, moderate or poor. Any side effects that occurred during the observation period were recorded. Statistical analyses were performed by the Mann–Whitney *U* test and p values <0.05 were considered significant.

Results

Of the 60 patients who took part in the study, the results for one were excluded because only one ampoule was administered. After decoding, both groups were found to be comparable with regard to sex, age, weight and height (Table 1).

Surgery lasted 73 minutes (SEM 5.5) in the epidural sufentanil group, compared to 83 minutes (SEM 6.2) in those given intramuscular buprenorphine. The times between the end of surgery and administration of analgesic were 128 minutes (SEM 11.1) and 123 minutes (SEM 12.1), respectively. The onset of pain relief was faster following epidural sufentanil, but not significantly so (Table 2). The quality of analgesia was significantly better during the first hour following epidural sufentanil but, after 4 hours, this group showed regression of pain relief which did not occur in those given buprenorphine (Fig. 1). Duration of analgesia was longer in the latter patients (Table 2).

Global assessment of pain relief was good or excellent in 72% of the sufentanil treated patients versus 60% of those in the buprenorphine group (Table 3). The difference was not statistically significant. Cardiovascular measurements remained stable in both groups (Fig. 2) and respiratory rates below 10 breaths/minute were not seen at any time (Fig. 3).

Side effects are shown in Table 4. The incidence of sedation was similar in both groups. Nausea and vomiting were reported by eight patients in the buprenorphine group compared to only one who received sufentanil.

Table 1. Patient data. Values expressed as mean (SEM).

	Group A 50 μg epidural sufentanil (n = 29)	Group B 0.3 mg intramuscular buprenorphine (n = 30)
Sex, F:M	13:16	13:17
Age, years	40.8 (2.8)	44.1 (2.9)
Weight, kg	70.5 (2.4)	67.1 (1.6)
Height, cm	170.7 (1.9)	170.2 (1.4)

Table 3. Global assessment of pain relief.

	Excellent	Good	Moderate	Poor
Group A 50 μg epidural sufentanil	13	8	4	4
Group B 0.3 mg intramuscular buprenorphine	10	8	6	6

No significant difference between groups (Mann–Whitney *U* test).

Table 2. Duration of surgery and onset and duration of pain relief. Values expressed as mean (SEM).

	Group A 50 μg epidural sufentanil	Group B 0.3 mg intramuscular buprenorphine	p*
Duration of surgery, minutes	72.9 (5.5)	82.7 (6.2)	NS
Time from end of surgery to analgesia, minutes	128.1 (11.1)	122.7 (12.1)	NS
Onset of pain relief, minutes	7.7 (1.0)	11.9 (1.9)	NS
Duration of pain relief, minutes	319.0 (24.2)	373.8 (27.2)	<0.05

* Mann–Whitney *U* test. NS, not significant.

Table 4. Side effects (number of patients).

	Group A 50 μg epidural sufentanil	Group B 0.3 mg intramuscular buprenorphine
Nausea	—	2
Vomiting	1	6
Sedation	9	8
Headache	—	1
Hypotension	—	1
Itching	2	—
Lacrimation	—	1
Urine retention	2	2

Discussion

The epidural administration of lipophilic opioids such as pethidine or fentanyl, is characterised by a more rapid onset of action but a shorter duration than found for hydrophilic compounds, for example, morphine.[6] Sufentanil, another highly lipophilic compound, appears to be no exception to this rule. Following an epidural injection of 50 μg it offers pain relief within 10 minutes, with a duration of approximately 5 hours.[1–3]

It was our hypothesis that because of the strong receptor binding capacity of sufentanil[7,8] the analgesic effect should last longer than pethidine and fentanyl, as has been shown for lofentanil, a compound with a similar chemical profile. However, the present findings confirm the published results[1–3] and suggest that physicochemical properties such as molecular weight, pka and lipid solubility influence the epidural analgesic action of the compound more than pharmacokinetic characteristics, receptor binding and interaction.

Compared to an intramuscular injection of buprenorphine, epidural sufentanil has the advantage of a better quality of pain relief during the first, most painful hours. It is efficacious for the first peak after orthopaedic postoperative pain[9] but further analgesia requires repeated injections. Titration according to patient needs, although not evaluated in this study, should be facilitated by its rapid onset of action.

The incidence of side effects, apart from sedation, was lower following sufentanil and it is also less compared to other opioids used epidurally after orthopaedic surgery.[10–12,13] The fact that four patients in the present study did not experience analgesia after epidural sufentanil is difficult to explain, especially when the results obtained with epidural sufentanil in previous studies[1–3] are considered. A possible reason might be migration of the catheter out of the epidural space when patients were moved from the operating table into bed.

In conclusion, epidural sufentanil 50 μg provided effective postoperative pain relief for 4–5 hours after orthopaedic surgery. The analgesic effect was shorter than that provided by buprenorphine 0.3 mg intramuscularly but was of better quality initially and associated with a lower incidence of side effects.

References

1. Donadoni R, Rolly G, Noorduin H, Vanden Bussche G. Epidural sufentanil for postoperative pain relief. *Anaesthesia* 1985; **40:** 634–8.
2. Verborgh C, Van der Auwera D, Van Droogenbroek E, Camu F. Epidural sufentanil for postsurgical pain relief. *European Journal of Anaesthesia* 1986; **3:** 313–20.
3. Van der Auwera D, Verborgh C, Camu F. Analgesic and cardiorespiratory effects of epidural sufentanil and morphine in man: a double-blind evaluation. *XIIth Congress of Anaesthesiology, Vienna (Austria), 7–13 September 1986.* In: Bergman H, Kramar H, Steinbereithner K. *Beitr. Anaesth. u. Intensivmed.* Wien: W. Maudrich Verlag, 1986; **17:** 253.
4. Rolly G, Versichelen L. Buprenorphine as postoperative analgesic. *Acta Anaesthesiologica Belgica* 1976; **27:** 183–6.
5. Harcus AH, Ward AE, Smith DW. Buprenorphine in postoperative pain: results in 7500 patients. *Anaesthesia* 1980; **35:** 382–6.
6. Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. *Anesthesiology* 1984; **61:** 276–310.
7. Leysen JE, Gommeren W, Niemegeers CJE. (^3H) Sufentanil, a superior ligand for mu-opiate receptors: binding properties and regional distribution in rat brain and spinal cord. *European Journal of Pharmacology* 1983; **87:** 209–25.
8. Colpaert FC, Leysen JE, Michiels M, Van den Hoogen RHWM. Epidural and intravenous sufentanil in the rat: analgesia, opiate receptor binding, and drug concentrations in plasma and brain. *Anesthesiology* 1986; **65:** 41–9.
9. Gjessing J, Tomlin PJ. Patterns of postoperative pain. A study of the use of continuous epidural analgesia in the postoperative period. *Anaesthesia* 1979; **34:** 624–32.
10. Barron DW, Strong JE. Postoperative analgesia in major orthopaedic surgery. Epidural and intrathecal opiates. *Anaesthesia* 1981; **36:** 937–41.

11. BILSBACK P, ROLLY G, TAMPUBOLON O. Efficacy of extradural administration of lofentanil, buprenorphine or saline in the management of postoperative pain. A double-blind study. *British Journal of Anaesthesia* 1985; **57:** 943–8.
12. GERIG HF, KERN F. Epidurales Buprenorphin für postoperative Analgesie nach Hüftoperationen. *Anaesthesia* 1983; **32:** 345–8.
13. STENSETH R, SELLEVOLD O, BREIVIK H. Epidural morphine for postoperative pain: experience with 1085 patients. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 148–56.

Anaesthesia, 1987, Volume 42, pages 1176–1179

The respiratory depressant effects of nalbuphine and papaveretum as intramuscular premedication

G. G. R. RUTTER, W. AVELING AND K. TUSIEWICZ

Summary

Forty-four patients scheduled for routine gynaecological surgery through a Pfannenstiel incision were given either nalbuphine or papaveretum as premedication, with hyoscine. Respiratory depression was measured by carbon dioxide rebreathing before and one hour after premedication. Both combinations produced significant respiratory depression as measured by the rebreathing test but no significant difference could be shown between the drugs in this respect.

Key words

Analgesics, narcotic; papaveretum, nalbuphine.
Measurement techniques; carbon dioxide response.

Nalbuphine is a narcotic agonist–antagonist of the phenanthrene series, synthesised in an attempt to provide optimal stimulation of opioid receptor subtypes. It has been shown in previous studies to have some advantages over morphine, including a ceiling to respiratory depression,[1] a lower incidence of nausea and vomiting[2] and a low abuse potential.[3] Nalbuphine appears relatively free of dysphoric effects, unlike some earlier agonist–antagonist drugs. Nalbuphine has been shown to be comparable with morphine when used as a premedicant.[4] It is also markedly sedative,[2] which could be considered beneficial postoperatively.

The trial was designed to compare the respiratory depressant effects of nalbuphine with those of papaveretum, as assessed by carbon dioxide rebreathing. Since a pilot study had shown unacceptable nausea and vomiting when nalbuphine was used as the sole premedicant, it was decided to include hyoscine in the premedication, as is the normal practice in our hospital with papaveretum.

Methods

Forty-six female patients of 16 years or over, scheduled for gynaecological operations via a Pfannenstiel incision, were allocated randomly to two groups. All were ASA grade 1 or 2 and all gave informed consent. Patients receiving opioids or antidepressants were not studied. The study was approved by the local ethical committee.

The control group received papaveretum and the trial group, nalbuphine; either drug was given in a dose of 0.3 mg/kg up to a maximum of 20 mg. The premedication was given intramuscularly with hyoscine, 0.4 mg/20 mg analgesic, 90 minutes pre-operatively.

Respiratory depression was assessed by a carbon dioxide rebreathing test before premedication and one hour after. This was based on a

---

G.G.R. Rutter, MB, BChir, FFARCS, Senior Registrar, W. Aveling, MB, BChir, FFARCS, K. Tusiewicz, MD, FFRACS, Consultants, Department of Anaesthesia, The Middlesex Hospital, London W1N 8AA.
Correspondence should be addressed to Dr W. Aveling please.

0003–2409/87/111176 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

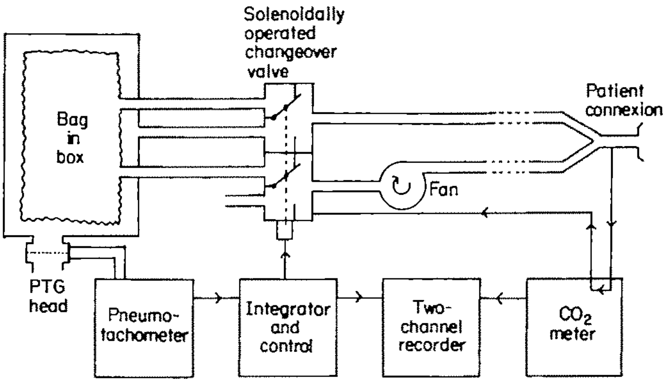


Fig. 1. Circuit for carbon dioxide rebreathing tests.

method described by Read,[5] with some detailed modifications mainly concerning the circuit (Fig. 1). This had two 1-metre tubes to the patient mouthpiece, with a circulating fan; this was convenient and also ensured good mixing of the gases in the rebreathing bag. The resistance of the system was acceptable; it was half that of a single tube. A solenoid operated changeover valve connected the patient either to air or to the rebreathing bag. Ventilation was measured by a Gould pneumotachometer, the Fleisch head of which was in the box around the bag and thus out of the patient system. The output of the pneumotachometer was rectified and integrated to give the total volume breathed each half minute; this was read as minute volume. Carbon dioxide concentration was continuously monitored at the mouthpiece by a Gould Mk4 capnometer.

The rebreathing test was performed with the patient in a consistent semirecumbent position. Initially the patient breathed room air for 2 minutes or as long as required to allow her to settle to normal ventilation and get used to the apparatus, after the hyperventilation shown by most patients when first connected to the circuit. The valve then automatically changed at end expiration to connect the patient to the rebreathing bag, which initially contained 6 litres 6% carbon dioxide in oxygen. The patient then rebreathed to 8 kPa CO_2 during runs of 3–5 minutes. The record obtained was read at half-minute intervals, ignoring the first; the ventilatory response to carbon dioxide was then calculated by linear regression using the least-squares criterion. A typical record is shown in Fig. 2.

Table 1. Patient data. Values expressed as mean (SD).

	Nalbuphine (n = 22)	Papaveretum (n = 22)
Weight, kg	59.7 (2.3)	62.6 (2.2)
Height, cm	162 (1.4)	162 (1.6)
Age, years	39.5 (2.2)	41.0 (2.5)

Table 2. Results of carbon dioxide rebreathing tests. Values expressed as mean (SD).

	Before premedication	After premedication
Slope (litres/minute/kPa)		
Nalbuphine	9.67 (0.871)	8.81 (0.925)
Papaveretum	11.58 (0.916)	10.15 (0.832)
Minute volume (litres) at 7.9 kPa CO_2		
Nalbuphine	22.1 (1.71)	17.9 (1.65)
Papaveretum	23.7 (1.66)	19.1 (1.69)

Statistical analysis of the tests was performed on the slopes and the interpolated minute volumes at 7.9 kPa CO_2. As ratios, the slopes could not be tested directly by Student's t-tests; they were therefore tested nonparametrically by Wilcoxon's rank test. The minute volumes were compared by Student's t-test.

Results

The two groups were similar in respect of age, weight and height (Table 1). Two patients were unable to perform the rebreathing test. Table 2 shows the mean results of the tests. No significant difference in either slope or minute volume at 7.9 kPa CO_2 was found between the nalbuphine and the papaveretum groups before premedication. Similarly, no significant difference between the groups in these variables was

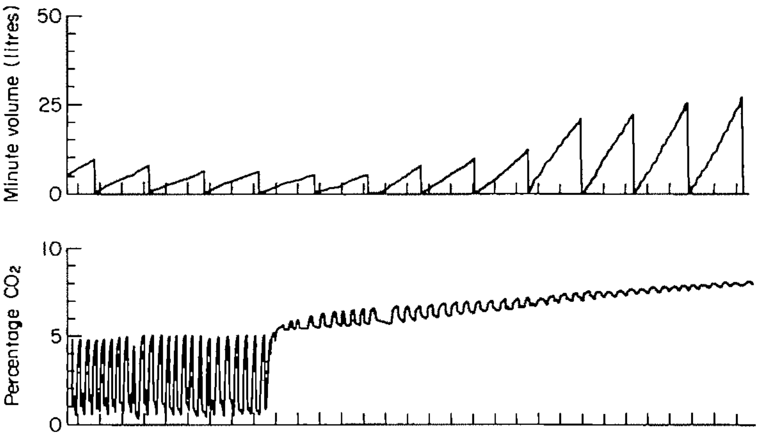


Fig. 2. Typical record from carbon dioxide rebreathing tests. The upper trace is of volume breathed, integrated over 30-second periods. The lower trace is of percentage carbon dioxide at the mouthpiece. The linear regression calculation yields slope = 1.94, minute volume at 7.9 kPa CO_2 = 24.6 litres, $r = 0.98$.

found after the premedication. However, on paired testing of results before and after premedication, a highly significant decrease in both slope ($p < 0.02$) and minute volume ($p < 0.01$) was found over the whole group after the premedication.

Discussion

The results show clearly that the carbon dioxide rebreathing test will detect the respiratory depression caused by premedicant doses of either drug. However, the test showed no significant difference between the two drugs. No account was taken of possible differences in the rate of absorption of the two agents but data provided by the manufacturers on the pharmacokinetics of nalbuphine[6] appear to indicate that absorption of this drug is similar to morphine, the major active constituent of papaveretum.

In a trial of this kind it is important to use equi-analgesic doses. The doses used were decided upon after a pilot study, and our own assessments of efficacy against postoperative pain confirmed that the doses were appropriate. Nalbuphine is a partial agonist and, unlike papaveretum, has a nonlinear dose–response relationship at least as regards respiratory depression. According to published data[7] the dose used should have just entered the flat part of the curve but, nevertheless, did not appear to offer any advantage in terms of respiratory depression.

The addition of another depressant, hyoscine, to the premedication could cloud the issue but would be expected to have the same effect in both groups. Moreover, the purpose of the trial was to compare the drugs in normal clinical use.

This study has shown nalbuphine to be an alternative to papaveretum for premedication, with the advantage that it is not a controlled drug. However, we were unable to show less respiratory depression than with a conventional opioid premedicant, papaveretum, in these healthy patients.

Acknowledgments

We would like to thank DuPont for financial support and Professor Semple for practical assistance with this study.

References

1. Romagnoli A, Keats AS. Ceiling effect for respiratory depression by nalbuphine. *Clinical Pharmacology and Therapeutics* 1980; **27**: 478–85.
2. Miller RR. Evaluation of nalbuphine hydrochloride. *American Journal of Hospital Pharmacy* 1980; **37**: 912–9.
3. Jasinski DR, Mansky PA. Evaluation of nalbuphine for abuse potential. *Clinical Pharmacology and Therapeutics* 1972; **12**: 78–90.
4. Pinnock CA, Bell A, Smith G. A comparison of nalbuphine and morphine as premedication agents for minor gynaecological surgery. *Anaesthesia* 1985; **40**: 1078–81.

5. READ DJC. A clinical method for assessing the ventilatory response to carbon dioxide. *Australasian Annals of Medicine* 1967; **16**: 20–32.
6. DU PONT. *Nubain (nalbuphine HCl): physician's monograph.* Garden City, New York: Endo Laboratories Inc.
7. GAL TJ, DIFAZIO CA, MOSCICKI J. Analgesic and respiratory depressant activity of nalbuphine: a comparison with morphine. *Anesthesiology* 1982; **57**: 367–79.

Anaesthesia, 1987, Volume 42, pages 1180–1182

The effect of rotation of an epidural needle

An *in vitro* study

B.H. MEIKLEJOHN

Summary

A study using postmortem dura mater demonstrated that rotation of the epidural needle significantly decreases the force required to puncture the dura. It is recommended that epidural needles should not be rotated after insertion of the tip into the epidural space.

Key words

Anaesthetic techniques; epidural.
Complications; dural puncture.

It has been suggested that rotation of the epidural needle within the epidural space may increase the risk of dural puncture.[1] This may occur with as little as 90° of rotation.[2] However, other authors have rejected this theory and have recommended that the needle should be rotated through 270°, with aspiration every 90°, in case the needle bevel lies partly within the dura but the flow of cerebrospinal fluid is prevented by a flap of dura.[3,4] This manoeuvre might detect such a situation but it might also core out a hole in the dura if the needle point has come to rest on the dura, putting it under tension. The present study was carried out to test the latter hypothesis.

Method

Sections of thoracolumbar dural sac were removed at postmortem from three adult spines. Each section was tested individually in the following manner.

The sac was divided into anterior and posterior strips and each strip was then cut into segments approximately 1.5 cm long. Anterior and posterior segments were selected randomly and mounted in a stage as illustrated in Fig. 1. They were placed onto the meniscus of Ringer lactate solution contained in a vessel, and clamped so as to be flat but not stretched. The longitudinal axis of the dura ran from left to right.

A Steriseal Oxford pattern Tuohy needle was supported in the vertical position by a guide that prevented lateral movement but presented minimal resistance to vertical movement. A platform, on which weights were placed, was fixed to the hub of the needle. Each needle was used for three measurements only, and a fresh segment of dura was used for each measurement.

Initial measurements were made for segments from each dural sac; weights were added until dural puncture occurred without needle rotation. Thereafter, smaller weights were used and the needle rotated clockwise using the needle wings. The weight applied and the amount of rotation required to puncture the dura were recorded. The results were analysed using linear regression analysis and Student's *t*-test.

B.H. Meiklejohn, BSc, MB, ChB, FFARCS, Lecturer, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

0003–2409/87/111180 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

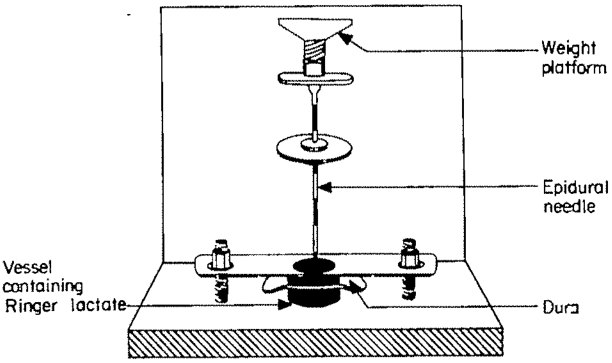


Fig. 1. Diagram of apparatus.

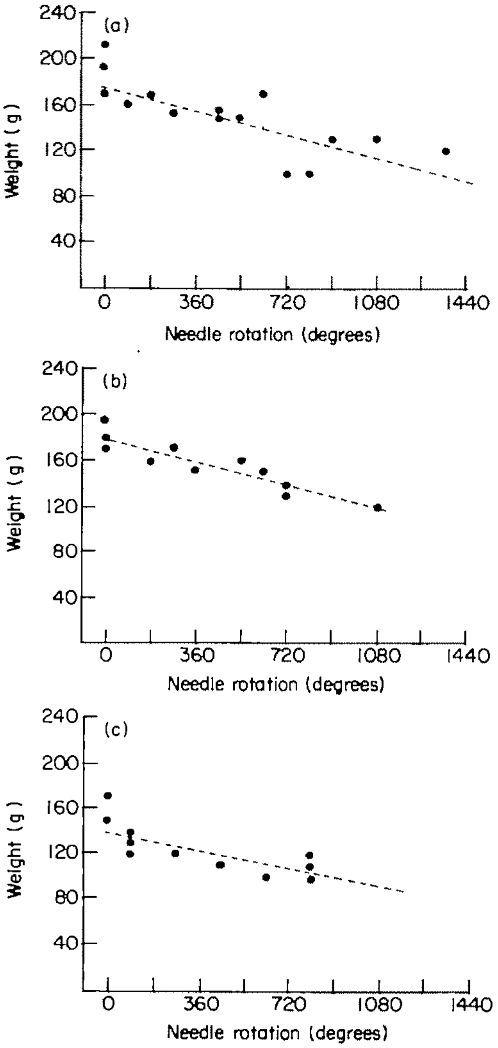


Fig. 2. Relationship between rotation and weight needed to puncture samples of dura from three sacs. (a) $r = -0.771$ ($p < 0.01$); (b) $r = -0.916$ ($p < 0.001$); (c) $r = -0.774$ ($p < 0.001$).

Results

A total of 40 segments of dura from three sacs (18, 11 and 11 segments respectively) were tested. The weight of needle and platform was constant at 11.5 g and ignored in the calculations. In each test, the weight of the needle indented the dura by 2–3 mm. The weights and rotations required for dural puncture are plotted in Fig. 2(a)–(c). There was a highly significant inverse correlation ($p < 0.01$ at least) for all three dural sacs between the amount of rotation and the weight required to puncture the dura. The weights required to puncture the dura were significantly less ($p < 0.01$) when the needle was rotated through 90–360° than when no rotation took place (Table 1).

Discussion

It is the practice of many anaesthetists to insert an epidural needle with the bevel parallel to and 'splitting' the fibres of the ligamentum flavum and then to rotate the bevel to face cephalad. Others[3,4] recommend routine rotation of the needle through 270°.

Modern disposable needles have sharp tips which could drill a hole in the dura if held against it, as may occur if the shaft of the needle is gripped by the dense interspinous ligaments, causing the tip to dimple the dura. This study set out to investigate whether an epidural needle should be moved after its tip has been positioned

Table 1. Weights required for dural puncture with and without rotation (*n*, number of experiments).

n	Rotation, degrees	Mean (SD) weight, g
8	0	180.9 (20.75)
11	90–360	148.6 (18.45)

in the epidural space. The results indicate that needle rotation increases significantly the risk of dural puncture.

The weight needed to pierce dura mater was surprisingly large but the fact that dural punctures occur in clinical practice is not in question. Apparent penetration of the dura by epidural catheters has been reported[5,6] but recent work suggests that this is unlikely unless the dura has already been breached by the needle.[7]

The methods used in the present study differ in some respects from the situation *in vivo* but these differences make dural puncture less likely in the *in vitro* preparation. Firstly, the dural tension in this study was kept as constant as possible. *In vivo*, dural tension is influenced by the curvature of the spine, position of the head and cerebrospinal fluid pressure. Secondly, if the dura is approached away from the midline, tethering of the dura by nerve roots may prevent it from being pushed away by the needle as it advances. Finally, when the needle lies in the epidural space, the ligaments, subcutaneous tissues and skin tend to resist further advancement of the needle. Rotation of the needle may overcome these forces and the needle may advance inadvertently into or through the dura.

Inadvertent dural puncture is at best an embarrassment and at worst, a life-threatening complication. All possible steps should be taken to avoid it. It is therefore recommended that once the needle has been inserted into the epidural space, with the bevel perpendicular to the fibres, it should not be moved for any reason other than to remove it.

Acknowledgments

The author thanks Dr A.R. Aitkenhead and Dr C.D. Hanning for their helpful advice and the pathologists at Leicester General Hospital for access to specimens.

References

1. Bromage PR. *Epidural analgesia*, 2nd edn. Philadelphia: W.B. Saunders, 1978.
2. Crowhurst PE. Accidental dural puncture. *Anaesthesia and Intensive Care* 1985; **13:** 213.
3. Moore DC. Accidental dural puncture—'Who has an eye on the end of the needle?' *Anaesthesia and Intensive Care* 1986; **14:** 208.
4. Moore DC. *Regional block*, 4th edn. Illinois: Thomas, 1965.
5. Park R. A migrating epidural cannula. *Anaesthesia* 1984; **39:** 289.
6. Robson JA, Brodsky JB. Latent dural puncture after lumbar epidural block. *Anesthesia and Analgesia* 1977; **56:** 725–35.
7. Hardy PAJ. Can epidural catheters penetrate dura mater? An anatomical study. *Anaesthesia* 1986; **41:** 1146–7.

Anaesthesia, 1987, Volume 42, pages 1183–1187

Subarachnoid block with hyperbaric lignocaine

A comparison with hyperbaric bupivacaine

M. C. EWART AND A. P. RUBIN

Summary

A double-blind study was carried out in 20 patients to compare 5% hyperbaric lignocaine and 0.5% hyperbaric bupivacaine for subarachnoid block. The injections were made in the lateral position and the patients turned supine immediately. The onset, extent and duration of sensory and motor blockade, the quality of anaesthesia, cardiovascular effects and the frequency of side effects were studied. Cephalad spread of analgesia was high (T_{4-5}) with both solutions. Bupivacaine produced a longer duration of action in the lumbar and sacral segments but the duration in the thoracic segments was similar. There was a considerable degree of hypotension in both groups but this responded readily to ephedrine. Hyperbaric lignocaine is an alternative to hyperbaric bupivacaine and its shorter duration of action in the lumbar and sacral segments is advantageous when a fast recovery is desirable.

Key words

Anaesthetic techniques, regional; spinal.
Anaesthetics, local; lignocaine, bupivacaine.

The withdrawal of cinchocaine (Nupercaine) in July 1985 has left a relative shortage of local anaesthetic agents suitable for subarachnoid anaesthesia. Glucose-free solutions seem to be unpredictable and may produce patchy blocks;[1–3] glucose-free 0.5% bupivacaine has been shown to be unsuitable for abdominal surgery, due to the low sensory block achieved.[4] They are, however, suitable for blocks confined to the lower extremities or perineum and especially for patients with painful conditions such as fractured neck of femur, who can be positioned with the painful side uppermost and then repositioned painlessly for operation within a few minutes.[5] Hyperbaric 0.5% bupivacaine has been investigated extensively;[4,6–8] 3 ml with 8% glucose is comparable to 1.5 ml 0.5% cinchocaine with 6% glucose[6] and is now widely used. This study was undertaken to determine the behaviour of hyperbaric lignocaine 5% with glucose monohydrate 7.5% compared to bupivacaine 0.5% with glucose monohydrate 8%.

Methods

Twenty patients (19 male) of ASA grades 1 and 2, aged 23–67 years and scheduled to undergo transurethral prostatic resection, inguinal herniorrhaphy, orthopaedic surgery of the lower limb or minor perineal surgery under subarachnoid block, were included in the study which was approved by the hospital ethical committee.

M.C. Ewart, MB, BS, FFARCS, Registrar, A.P. Rubin, MB, BChir, FFARCS, Consultant, Department of Anaesthesia, Charing Cross Hospital, London W6 8RF.
Correspondence should be addressed to Dr M.C. Ewart, Anaesthetic Registrar, The Hospital for Sick Children, Great Ormond Street, London WC1N 3BR.

0003–2409/87/111183 + 05 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Informed consent was obtained from each patient.

Papaveretum 0.3 mg/kg to a maximum of 20 mg with hyoscine 0.06 mg/kg was given intramuscularly 1–2 hours before the lumbar puncture. An intravenous infusion was established and the circulation preloaded with 500 ml Hartmann's solution. The patients were then placed in the left lateral horizontal position and lumbar puncture performed in the $L_{3/4}$ space using a midline approach with a 25- or 22-gauge needle. They were randomly allocated to receive either 3 ml 0.5% bupivacaine in 8% glucose or 1.5 ml 5% lignocaine in 7.5% glucose. The lignocaine solutions were obtained from Astra Pharmaceuticals Ltd. Once a free flow of clear cerebrospinal fluid was obtained, the test solution was injected at a rate of 1 ml every 4–5 seconds without barbotage, the needle withdrawn and the patient turned supine immediately.

One anaesthetist administered the solutions and the other, who was unaware of the drug used, evaluated the blocks. The cephalad spread of sensory block, degree of motor block of the lower limbs, arterial pressure and heart rate were recorded every 2 minutes until sensory and motor block were unchanged for four consecutive readings. The level of sensory block was assessed using the blunt end of a Sherwood B400 27-gauge dental needle. The degree of motor block was assessed on the Bromage 0–3 scale:[9] 0, no motor block; 1, inability to raise the extended leg (just able to move the knees); 2, inability to flex the knees (able to move feet only); and 3, inability to flex the ankle joint (unable to move feet or knees).

When the block was complete, the patient was positioned for the required surgery. Pulse rate and arterial blood pressure were recorded at 5-minute intervals. The quality of anaesthesia and the need for any additional medication, in the form of diazepam for sedation or general anaesthesia if the operation outlasted the block, were recorded. Ephedrine was given for hypotension (systolic blood pressure pressure less than 95 mmHg) and atropine for bradycardia (heart rate less than 50 beats/minute) without hypotension.

Further assessments of sensory and motor block were made at 15-minute intervals in the recovery period until there was no demonstrable sensory or motor loss. The patients were visited on the following day for signs of possible complications.

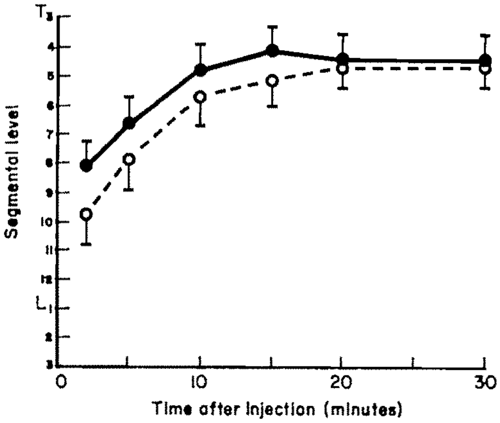


Fig. 1. Onset of analgesia (mean, SEM): ●, lignocaine; ○, bupivacaine.

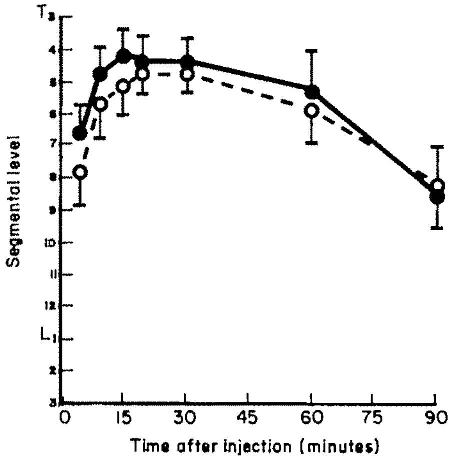


Fig. 2. Segmental spread of analgesia (mean, SEM): ●, lignocaine; ○, bupivacaine.

Differences between means were analysed by Student's *t*-test and differences between proportions by Fisher's exact test; $p < 0.05$ was taken to indicate a significant difference.

Results

There were no significant differences between the patients in the two groups with respect to age, weight, height, sex or needle size used.

Sensory block

Onset (Fig. 1). The mean onset times for analgesia to a level of T_{12} were less than 2 minutes with both solutions. The mean times

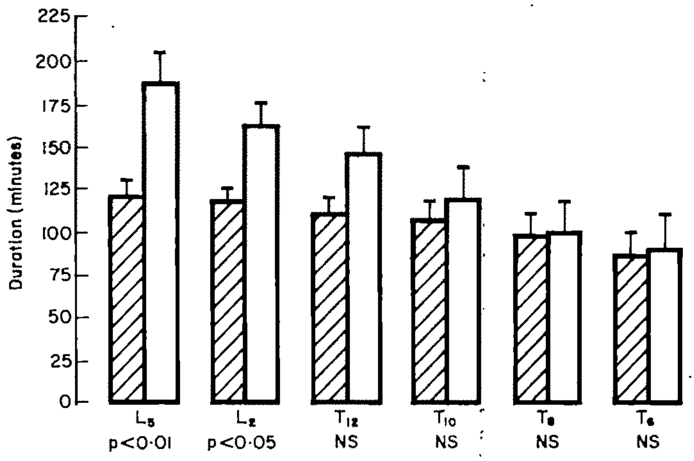


Fig. 3. Duration of analgesia (mean, SEM): ▨,lignocaine; □, bupivacaine. NS, Not significant.

Table 1. Maximum spread of analgesia.

	Drug	
Segmental level	Lignocaine	Bupivacaine
Higher than T_1	1	0
T_1–T_5	8	9
T_6–T_9	0	1
Lower than T_9	1	0

until the spread of analgesia was maximal, were between 15 and 20 minutes; there was no significant difference between the two solutions.

Spread (Fig. 2). The mean maximum spread of analgesia for both solutions was between T_4 and T_5. Table 1 illustrates the scatter of maximum levels of analgesia. There was one very high block (C_7) and one rather low block (T_{10}) in the lignocaine group.

Duration (Fig. 3). The mean duration of block at the T_6–T_{10} levels was very similar for the two groups: about 90 minutes at the T_6 level and about 115 minutes at the T_{10} level. At the lumbar and sacral segments, however, the blocks lasted significantly longer in the bupivacaine group, about 190 minutes at L_5 compared to 120 minutes for the lignocaine group ($p < 0.01$).

Motor block

Onset and degree. No differences were found with regard to onset times for motor block or frequencies of different degrees of motor block between the two groups. The mean time for complete motor block was about 7 minutes.

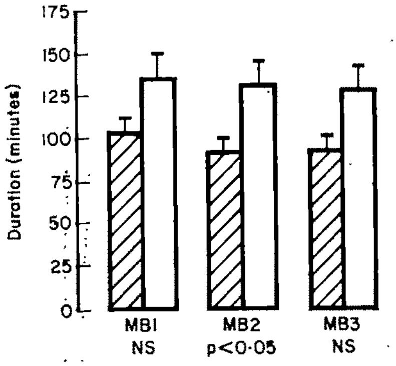


Fig. 4. Duration of motor block (mean, SEM): ▨, lignocaine; □, bupivacaine. NS, Not significant; MB, motor block.

Duration (Fig. 4). The mean duration of almost complete motor block (grade 2 on the Bromage scale) was significantly longer for bupivacaine (132 minutes) than for lignocaine (93 minutes). The durations of grade 1 and 3 motor block were also longer for bupivacaine but the difference did not reach statistical significance.

Cardiovascular changes

No significant differences were found between the groups with regard to maximum percentage decrease in heart rate, systolic or diastolic arterial blood pressure during the first 30 minutes after administration of the local anaesthetic. Systolic arterial pressure decreased by a mean of 31% in the bupivacaine group and 25% in the lignocaine group. Vasoactive drugs were given for hypotension or bradycardia in eight of the bupivacaine group and six of the lignocaine group during the first 30 minutes.

Quality of anaesthesia

Two patients in the lignocaine group and one in the bupivacaine group had blocks of insufficient duration. The first patient in the lignocaine group, who underwent transurethral resection, complained of mild discomfort after 95 minutes and felt the insertion of the urinary catheter. The second patient in the lignocaine group, who underwent transurethral resection and hydrocele repair, complained of pain in the right hip after 52 minutes and was given a general anaesthetic. The patient in the bupivacaine group who underwent inguinal herniorrhaphy, complained of pain after 120 minutes and was given a general anaesthetic.

Adverse reactions

Each patient was visited on the day after the operation. There were no postspinal headaches or other complications.

Discussion

Hyperbaric lignocaine is widely used for subarachnoid blocks outside the United Kingdom but there are few reports about its characteristics. Previous studies had suggested 3 ml as a suitable volume of hyperbaric bupivacaine[6–8] and 1.5 ml for hyperbaric lignocaine.[10,11] In many regional techniques lignocaine seems to have a faster onset than bupivacaine but we were unable to show any difference between the two as spinal solutions.

We have shown that both hyperbaric solutions produce high blocks; nine out of ten patients in each group developed a block above the T_6 dermatome. High blocks seem, therefore, to be a feature of hyperbaric spinal solutions rather than a particular property of lignocaine. There have been two reports of the high spread of hyperbaric 5% lignocaine, one of respiratory depression and arrest[12] and the other of cervical and bulbar nerve involvement which led to sedation and dysphagia.[10] We saw no such consequences and it is interesting that these side effects occurred either in obese women who, when placed on their sides, had a distinct head-down spinal slope, or in pregnancy, when the gravid uterus may well cause aortocaval compression and alter cerebrospinal fluid dynamics.

The most interesting result is the similar duration of action of lignocaine and bupivacaine in the thoracic dermatomes T_6–T_{12}. Only in the lumbar and sacral segments was bupivacaine found to be of longer duration. Millar *et al.*[10] found the longer duration of plain 0.5% bupivacaine to be advantageous, in that it led to a significant reduction in postoperative analgesic requirements following transurethral resection. This advantage must, of course, be weighed against the longer duration of numbness and immobility of the legs, which is a common cause of patient dissatisfaction.[10] Perhaps bupivacaine would be the best agent for transurethral resection in that it provides adequate duration for the operation and prolonged analgesia in the lumbar and sacral segments, which allows complications such as postoperative clot retention to be managed painlessly.

The onset of motor block was similar in both groups and followed the onset of sensory block. The duration of motor block was longer for bupivacaine than for lignocaine although this was found to reach statistical significance only at the grade 2 level. Motor block in the legs was of shorter duration than sensory block in the lumbar and sacral segments. These results seem to confirm the principle that motor nerves are more difficult to block than sensory nerves, which is of obvious importance in order to avoid the unpleasant feeling of residual motor block with normal sensation.

Despite a moderate fluid preload of the circulation, bradycardia and hypotension were seen frequently in both groups of patients but were easily treated with either intravenous atropine or ephedrine. Two patients, one in each group, developed hypotension after the end of the operation and this was probably related to the lowering of the legs from the lithotomy position. In one of these patients the hypotension occurred after arrival in the recovery area. It is obviously important that arterial pressure is monitored frequently until the block has worn off completely.

Hyperbaric lignocaine is a useful alternative for urological, lower abdominal and lower limb surgery. It would be particularly advantageous when early recovery is indicated.

Acknowledgments

We would like to thank Mr H.H. Edstrom for his valuable assistance in the statistical analysis for this work, and our surgical colleagues for allowing us to study their patients.

References

1. MOORE DC. *Regional block*, 4th edn. Springfield: Charles C. Thomas, 1965.
2. CAMERON AE, ARNOLD RW, GHORIS MW, JAMIESON V. Spinal analgesia using bupivacaine 0.5% plain. Variation in the extent of the block with patient age. *Anaesthesia* 1981; **36:** 318–45.
3. BROWN DT, WILDSMITH JAW, COVINO BG, SCOTT DB. Effect of baricity on spinal anaesthesia with amethocaine. *British Journal of Anaesthesia* 1980; **52:** 589–96.
4. CHAMBERS WA, EDSTROM HH, SCOTT DB. Effect of baricity on spinal anaesthesia with bupivacaine. *British Journal of Anaesthesia* 1981; **53:** 279–82.
5. TATTERSALL MP. Isobaric bupivacaine and hyperbaric amethocaine for spinal analgesia. A clinical comparison. *Anaesthesia* 1983; **38:** 115–9.
6. CUMMINGS GC, BAMBER DB, EDSTROM HH, RUBIN AP. Subarachnoid blockade with bupivacaine. A comparison with cinchocaine. *British Journal of Anaesthesia* 1984; **56:** 573–9.
7. SUNDNES KO, VAAGENES P, SKRETTING P, LIND B, EDSTROM HH. Spinal anaesthesia with hyperbaric bupivacaine; effects of volume of solution. *British Journal of Anaesthesia* 1982; **54:** 69–74.
8. CHAMBERS WA, LITTLEWOOD DG, EDSTROM HH, SCOTT DB. Spinal anaesthesia with hyperbaric bupivacaine: effects of concentration and volume administered. *British Journal of Anaesthesia* 1982; **54:** 75–80.
9. BROMAGE PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1965; **16** (Suppl.): 55–69.
10. MILLAR JM, JAGO RH, FAWCETT DP. Spinal analgesia for transurethral prostatectomy. Comparison of plain bupivacaine and hyperbaric lignocaine. *British Journal of Anaesthesia* 1986; **58:** 862–7.
11. BEMBRIDGE M, MACDONALD R, LYONS G. Spinal anaesthesia with hyperbaric lignocaine for elective Caesarean section. *Anaesthesia* 1986; **41:** 906–9.
12. FISHER A, BRYCE-SMITH R. Spinal analgesic agents. A comparison of cinchocaine, lignocaine and prilocaine. *Anaesthesia* 1971; **26:** 324–9.

Anaesthesia, 1987, Volume 42, pages 1188–1190

Tracheal versus intravenous atropine

A comparison of the effects on heart rate

B. M. BRAY, H. M. JONES AND E. M. GRUNDY

Summary

Atropine 600 μg was given either intravenously or intratracheally and the change in heart rate noted in a double-blind, randomised study of 40 anaesthetised patients. There was no significant difference between the two groups in the maximum increase in heart rate, 20.3 beats/minute in the tracheal compared to 21.4 beats/minute in the intravenous group. However, the maximum increase occurred significantly earlier in the tracheal group, 45.5 seconds after administration compared to 95.5 seconds in the intravenous group (p < 0.01, 95% confidence interval 36.8–63.2 seconds). This study supports the clinical observation that tracheal and intravenous atropine are equally effective and suggests that the trachea should be the route of choice when a rapid response is required.

Key words

Lung; trachea.
Parasympathetic nervous system; atropine.

The tracheal route for drug administration was first reported by Redding[1] in 1967 and a technique for delivery by this route has been described which involves deposition of the drug beyond the distal end of the tracheal tube followed by 5–10 forceful ventilations.[2] This route is mentioned in the 1986 American Heart Association *Standards and Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiac Care*[3] and is a route currently recommended by the Resuscitation Council in the UK.[4] Most studies of this route have been based on animal models and there are a few human case reports. This study compares the effects of atropine 600 μg administered via the tracheal route with the same dose administered intravenously.

Methods

All patients were scheduled to undergo elective gynaecological or surgical procedures that necessitated tracheal intubation and muscular relaxation. The study was approved by the hospital ethical committee.

The patients received lorazepam 2–4 mg orally approximately 2 hours prior to surgery. Anaesthesia was induced with thiopentone 4–6 mg/kg and tracheal intubation facilitated with vecuronium 80 μg/kg. Anaesthesia was maintained with fentanyl 1–2 μg/kg, enflurane 1–3% and nitrous oxide 66% in oxygen delivered via a Manley ventilator. The heart rate was monitored with a Rigel 302 electrocardiograph, which provides a digital readout of heart rate updated every 4 seconds.

B.M. Bray, FFARCS, Registrar, H.M. Jones, FFARCS, Senior Registrar, E.M. Grundy, MRCP, FFARCS, Consultant, Department of Anaesthesia, The Middlesex Hospital, Mortimer Street, London W1N 8AA.
Correspondence should be addressed to Dr B.M. Bray, Room 107, The Rayne Institute, University Street, London WC1E 6JJ.

0003–2409/87/111188 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

The patients were randomly allocated into two groups. Group A simultaneously received 1 ml 0.9% saline into the trachea and 1 ml (600 μg) atropine intravenously. Group B received the reverse combination. The 1 ml of solution was delivered into the trachea via a fine bore catheter as described previously[5] and immediately followed by five manual hyperinflations of the lungs to disseminate the solution. Intravenous injections were given through a needle sited in a vein on the dorsum of the hand and immediately flushed with saline.

Pulse rate was recorded at 3, 2, 1 and 0 minutes prior to drug administration and thereafter at 15-second intervals for 2 minutes and then every minute for 10 minutes. In addition, the peak heart rate and the delay from time of drug administration were noted. The data were analysed using the unpaired *t*-test and 95% confidence intervals calculated.

Results

Forty patients were studied, 20 in each group. All were ASA grade 1 and were between 20 and 60 years of age. There were no significant differences between the two groups and the details are shown in Table 1.

Data on the changes in heart rate are summarised in Table 2. There was no significant difference in the maximum increase in heart rate between the two groups: a 20.3 beats/minute increase in the intraveneous group compared to 21.4 beats/minute in the tracheal group. However, the maximum increase occurred significantly earlier when atropine was given by the tracheal route (Fig. 1); 95.5 seconds to the maximum increase in the intravenous group, compared to 45.5 seconds when atropine was given via the tracheal route ($p < 0.01$, mean difference 50 seconds, 95% confidence interval 36.8–63.2 seconds).

Table 1. Details of patients.

	Group A ($n = 20$)	Group B ($n = 20$)
Mean age (range), years	37.6 (20–55)	37.1 (20–55)
Sex, F: M	15:5	13:7

The heart rate returned to pre-injection levels significantly more quickly in the tracheal group: 4.3 minutes after injection compared to 8.8 minutes in the intravenous group ($p < 0.05$, mean difference 4.68 minutes, 95% confidence interval 3.50–5.79 minutes).

Discussion

The production of a reflex tachycardia from direct tracheal stimulation would augment the pharmacological effects of atropine. However, the administration of 5 ml 0.9% saline into the trachea of baboons has been shown to produce no increase in heart rate.[6] Our study was designed so that direct tracheal stimulation was the same in all patients, since both groups received 1 ml of solution into their tracheas as part of the protocol.

Kradjan[7] showed that therapeutic blood levels could be obtained following inhalation of a single metered dose of atropine by aerosol, but this involved a variable amount of raining out in the upper airway. The presence of a tracheal tube avoids this problem and it has been shown in intubated dogs that manual hyperinflation is required to distribute radiological contrast material symmetrically and to the lung periphery.[2]

Table 2. Comparison of changes in heart rate, time to maximum heart rate and time to recover pre-atropine heart rate after atropine 600 μm given intravenously (Group A) or tracheally (Group B). Values expressed as mean (SD). Data analysed using unpaired *t*-test.

	Group A	Group B	Difference (95% confidence interval)	p value
Maximum increase in heart rate, beats/minute	21.4 (10.3)	20.3 (9.6)	1.1 (−4.89–7.89)	NS
Time to maximum heart rate, seconds	95.5 (32.2)	45.5 (18.3)	5.0 (36.8–63.2)	$p < 0.01$
Time to recover heart rate, minutes	8.8 (1.6)	4.3 (1.8)	4.7 (3.50–5.79)	$p < 0.01$

NS, Not significant.

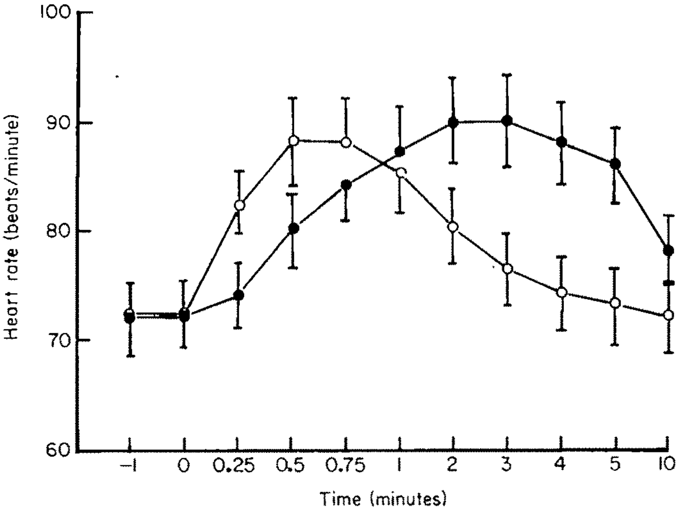


Fig. 1. Mean (SEM) heart rate following administration of atropine 600 μg via tracheal and intravenous routes. O, Tracheal; ●, intravenous.

Atropine is administered for its vagal blocking activity reflected by its chronotropic effect, which we took as a marker of systemic absorption. Our results show that atropine 600 μg produced the same increase in heart rate whether administered intravenously or via the tracheal route. It is of greater interest that it produced this change in about half the time. With rapid absorption from the tracheobronchial tree, it can be speculated that this represents a left heart circulation time for tracheal administration as opposed to a left and right heart circulation time for intravenous administration. The onset of action as measured by the time to maximum heart rate, would be shorter if the intravenous injection was into a central vein rather than into a vein on the dorsum of the hand. However, a hand to heart circulation time would not be expected to exceed 10 seconds and this would not greatly affect the difference between the two groups.

The administration of atropine to a patient is a routine part of many anaesthetic techniques and can be required in an emergency. Previous reported experience of tracheal administration of atropine consists of case reports in a resuscitation situation.[8] These results confirm the clinical efficacy of tracheal atropine in anaesthetised patients and thus that the tracheal route should be considered in patients with difficult intravenous access. It is the route of choice when a rapid clinical response is desired, as in an emergency.

References

1. Redding JS, Asuncion JS, Earson JW. Effective routes of drug administration during cardiac arrest. *Anesthesia and Analgesia* 1967; **46:** 253–8.
2. Greenberg MI, Spivey WH. Comparison of deep and shallow endotracheal administration of Dionosil in dogs and the effect of manual hyperventilation. *Annals of Emergency Medicine* 1985; **14:** 209–12.
3. American Heart Association. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). Parts 3 and 4. *Journal of the American Medical Association* 1986; **255:** 2933–69.
4. Resuscitation Council (UK). *Poster on cardiopulmonary resuscitation.* Department of Anaesthetics, The Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Rd, London, 1984.
5. Jones HM, Bray B. Endotracheal administration of drugs. *Anaesthesia* 1985; **40:** 921.
6. Chernow B, Holbrook P, D'Angona DS, Zaritsky A, Casey LC, Fletcher JR, Lake CR. Epinephrine absorption after intratracheal administration. *Anesthesia and Analgesia* 1984; **63:** 829–32.
7. Kradjan WA. Serum atropine concentration after inhalation of atropine sulfate. *American Review of Respiratory Disease* 1981; **123:** 471–2.
8. Greenberg MI, Mayeda DV, Chrzanowski R, Brumwell D, Baskin SI, Roberts JR. Endotracheal administration of atropine sulfate. *Annals of Emergency Medicine* 1982; **11:** 546–8.

Anaesthesia, 1987, Volume 42, pages 1191–1196

CASE REPORT

Hepatotoxicity and death following two enflurane anaesthetics

J. D. PAULL AND D. W. FORTUNE

Summary

A 67-year-old woman died with massive fatty change in the liver 41 hours after her second enflurane anaesthetic in 28 days. The clinical features of five previously reported similar deaths are summarised. Possible mechanisms of the hepatotoxicity are reviewed briefly.

Key words

Anaesthetics, volatile; enflurane.
Liver; toxicity.

Enflurane was discovered in 1963. By 1981 it was estimated that more than 20 million patients had received the agent and 10 cases had been reported in which enflurane was incriminated as a cause of hepatic toxicity.[1–10] In 1983, Lewis *et al.*[11] reviewed 24 cases of hepatotoxicity, of which seven had been included in previous reports; five of the 24 patients died. No fatalities have been reported since 1980.

The case reported here was revealed in a mortality review conducted in this department. It occurred in 1976. It is reported now because of the relative rarity of fatal hepatic necrosis following enflurane administration and because of the speed with which the hepatotoxic change developed.

Case history

A 67-year-old, Lebanese-born woman was admitted for diagnostic curettage because of postmenopausal bleeding. She had received a general anaesthetic in Lebanon many years previously for a Caesarean section. She did not know what anaesthetic agents had been administered on that occasion.

Five years before the present admission she had suffered a myocardial infarction and, for the 3 months preceding admission, she had been treated with digoxin 0.125 mg twice daily for mild cardiac failure. She had taken indomethacin 25 mg t.d.s. for 18 months.

Pre-operatively she was noted to be obese and afebrile. Her pulse rate was 100 beats/minute with occasional extrasystoles, the arterial pressure was 150/80 mmHg and the jugular venous pressure was not elevated. The apex beat was displaced to the 5th left intercostal space in the anterior axillary line; she had normal heart sounds and a murmur consistent with aortic sclerosis. There were no adventitial sounds in the chest and no peripheral oedema. She had a lower midline abdominal scar and there is no record to indicate whether the liver or spleen was palpable.

J.D. Paull, MB, BS, FFARACS, Dip Ed, Director of Anaesthesia, D.W. Fortune, MB, ChB, FRCP(Edin), FRC Path, FRCPA, FIAC, Director of Pathology, The Royal Women's Hospital, 132 Grattan St, Melbourne 3053, Australia.

0003–2409/87/111191 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Chest X ray showed a markedly enlarged heart and pulmonary vascular engorgement but no parenchymal disease. Her ECG showed sinus rhythm with occasional ventricular ectopic beats and evidence of old inferior infarction.

After premedication with morphine 7.5 mg and atropine 0.6 mg intramuscularly she had a general anaesthetic of 15 minutes' duration for diagnostic curettage. Anaesthesia was induced with thiopentone 125 mg and nitrous oxide and oxygen were supplied, each at a rate of 1 litre/minute, via a circle system. Enflurane was given from a Goldman vaporizer in the inspiratory limb. Earlier on the same day, halothane had been used in the breathing system. Curettage revealed adenomatous hyperplasia with no evidence of malignancy.

The patient made an uneventful recovery and went home 24 hours later. Her temperature was recorded on two occasions postoperatively and was normal. She did not vomit or complain of nausea, and no rash or jaundice were noted.

She was readmitted subsequently for abdominal hysterectomy, which was carried out 28 days after the previous operation. At examination prior to hysterectomy, the clinical findings were identical to those recorded previously and a further ECG and chest X ray were unchanged. The haematological and biochemical findings are summarised in Table 1. It was not known whether the patient had previously received a blood transfusion but she was hepatitis Australia antigen (HAA) negative when tested. She had no antibodies on screening and was not given blood or blood products during her hospitalisation.

Following premedication with morphine 7.5 mg and atropine 0.6 mg intramuscularly, general anaesthesia was induced with thiopentone 150 mg, and pancuronium 4 mg was administered. A tracheal tube was inserted and her lungs were ventilated manually with a gas mixture that comprised nitrous oxide 4 litres/minute and oxygen 2 litres/minute and enflurane. The enflurane was administered from a Mark 2 Enfluratec (Cyprane). The percentage of enflurane used was not recorded but at that time it was common practice to use 1–1.5%. We believe that although new breathing system tubing was used, parts of the anaesthetic machine might have been contaminated with halothane from use on previous occasions. Abdominal hysterectomy and bilateral salpingo-oophorectomy were performed; the procedure lasted 90 minutes. Forty-five minutes after induction, she was given a supplement of 50 mg thiopentone and 1 mg pancuronium. She received one litre of Ringer lactate solution during the operation and blood loss was minimal. Her systolic arterial pressure ranged from 160 to 200 mmHg and her pulse rate varied from 110 to 130 beats/minute. ECG monitoring was used and no change in the ECG was noted.

After reversal of neuromuscular blockade with atropine 1.2 and neostigmine 2.5 mg, her trachea was extubated and she spent 30 minutes in the recovery room, during which time she received intranasal oxygen at 2 litres/minute. On return to the ward she was conscious but

Table 1. Haematological and biochemical data prior to curettage and on the first day after hysterectomy.

	Before curettage	After hysterectomy	Normal values
Na^+ (mmol/litre)	135	139	132–146
K^+ (mmol/litre)	3.9	3.9	3.5–5.5
HCO_3^- (mmol/litre)	28	28	20–26
Urea (mmol/litre)	3.7	11.5	1.70–6.70
Uric acid (mmol/litre)	0.33	0.61	0.14–0.42
Serum creatinine (mmol/litre)	0.07	0.14	0.03–0.11
Haemoglobin (g/litre)	119	116	110–150
White cell count ($\times 10^9$/litre)	9.0	13.0	4.0–10.0
Comment	Iron deficiency	Toxic film Shift to left	
Blood group	O Rh positive		
HAA	Negative		

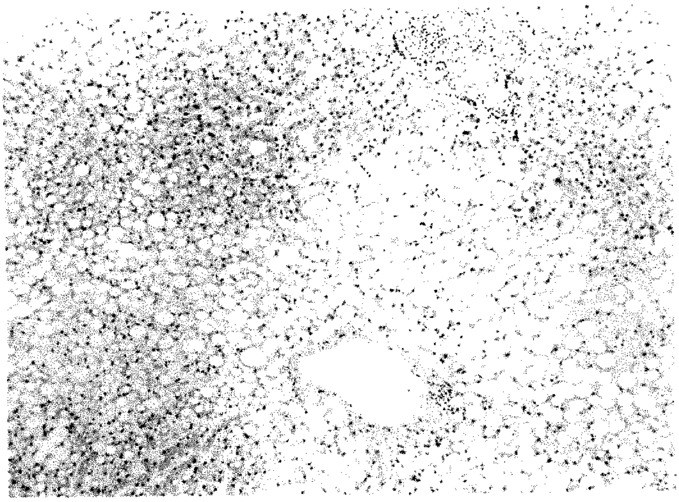


Fig. 1. Liver showing severe fatty change in centrilobular zone. The parenchymal cells in the periportal zone are less severely affected. H&E × 100.

drowsy, and responded to spoken commands. Postoperatively she required a total of three doses of morphine 7.5 mg intramuscularly for pain relief.

Six hours postoperatively her oral temperature was noted to be 38°C and she had a tachycardia of 128 beats/minute. This was thought to indicate sepsis and penicillin 1 megaunit and sulphadimidine 1 g 6-hourly by intramuscular injection were prescribed. The following morning she was described as 'looking toxic' and a blood culture was taken. The sulphadimidine was discontinued and gentamicin prescribed in a dose of 80 mg 8-hourly intravenously. She was noted to have some basal crepitations but her jugular venous pressure was not elevated. A full blood examination revealed a haemoglobin of 116 g/litre and a white cell count of 13.0×10^9/litre, with 9.75×10^9/litre neutrophils of which 19% were band forms. The white cells showed toxic granulation suggestive of an infection. There were 0.8×10^9/litre monocytes and 2.5×10^9/litre lymphocytes. Her ECG showed a sinus tachycardia without ventricular ectopics and there was no change in the infarct pattern noted previously.

At 22:00 hours on the second postoperative day her oral temperature was 38.7°C and she was noted to be occasionally restless. At 04:00 hours her temperature was 38.0°C and the pulse rate was 140 beats/minute. At 05:00 hours she was found dead.

Postmortem

The significant postmortem findings are presented. There was no icterus. The heart weighed 560 g and showed hypertrophy of the left ventricle with scarring and fibrosis in the posterolateral wall. The aortic valve cusps were sclerotic. The coronary ostia and the coronary arteries showed no narrowing or occlusion. Both lungs were heavy and displayed intense congestion in the posterior basal segments of both lobes.

The liver weighed 2.5 kg and had a pale and shrunken capsular surface. The cut surface was fatty and had a mottled appearance; darker zones around the portal vein tributaries were interspersed with pale yellow zones. The gall bladder contained two mulberry stones and three facetted stones. There was no blood in the peritoneal cavity. Microscopically, the liver showed massive fatty change. No evidence of inflammation was seen (Fig. 1).

Discussion

Death due to hepatic necrosis following enflurane exposure is rare. In the review by Lewis *et al.*[11] only five deaths were recorded and none has been reported since 1980. The clinical features of those five cases and of the present case are summarised in Table 2. Lewis *et al.*[11] selected 24 from a total of 58 published and privately reported cases of suspected enflurane hepatitis;

Table 2. Clinical data from this case (1976) and from the five fatal cases reported by Lewis *et al.*[11]

Year	Age	Sex	Operation	Duration of enflurane anaesthesia (minutes)	Previous exposure (days before)	Time to onset of symptoms	Time to onset of jaundice	Fever present	Eosino-philia	Liver histology
1976	67	F	Curettage	15	—				+	
			Abdominal hysterectomy	90	Enflurane (28)	6 hours	(none)	+	−	Massive fatty change, few surviving cells
1977	65	M	Colectomy	?						
			Laparotomy	?	Enflurane (14)					
			Laparotomy	?	Enflurane (35)	?	?	?	?	Massive centrilobular necrosis
1977	45	M	Anal fissurectomy	90	None	7–9 days	14 days	?	−	Massive necrosis
1978	55	M	Cholecystectomy	105	?	2 days	4 days	+	−	Centrilobular necrosis and fatty change
1979	30	F	Rhinoplasty	130	Halothane (21)	24 hours	?	+	+	Massive necrosis
1980	85	F	Cataract removal	120	—					
			Iris repair	150	Enflurane (25)	7 days	7 days	+	−	Submassive centrilobular necrosis

only those cases in which there was no serological, clinical or histological evidence of viral hepatitis, no other hepatotoxic drug exposure and no other recognisable or tenable cause of postoperative jaundice, were included. In their opinion, the five deaths which they reported met those criteria.

The features of the present case which suggest that enflurane was the causative agent, include the repeated exposure, the negative HAA test and the absence of histological signs of inflammation in the liver. The high fever and lack of any other acute systemic illness are also suggestive. The speed of onset of the hepatic destruction is remarkable and, no doubt, accounts for the absence of clinically detectable jaundice. She was not hypotensive or clinically hypoxic at any time during or after her operation, and received supplemental oxygen intranasally for one hour postoperatively. The high rate–pressure product noted during the second procedure was most likely to have been the result of light anaesthesia. It is conceivable that it was the result of an intercurrent illness but no evidence of this was obtained at the pre-operative clinical examination.

Factors which might have caused pre-existing liver damage were her cardiac failure, which may result in cirrhosis, and her consumption of indomethacin. However, there is little evidence to suggest that these two factors were of any significance. The cardiac failure was mild, required only digoxin treatment and was of recent onset; it had been treated for only 3 months. There was no histological evidence of hepatic cirrhosis. There have been no reports of indomethacin as a cause of hepatic failure.[12]

In 19 of the 24 cases reviewed by Lewis *et al.*,[11] fever was the presenting symptom and, in the majority, the onset was within 72 hours. The temperature in the present case increased to 38°C within 6 hours of operation, with no clinical or postmortem evidence of sepsis. The blood culture was negative.

The durations of this patient's exposures to enflurane (15 and 90 minutes) were shorter than the mean exposure time of 2.2 hours in the cases reported by Lewis *et al.*[11] (Table 2). There was no biochemical evidence of liver failure in our patient because the clinical picture led the attending physician to believe that sepsis was the cause of her illness, and hepatic enzyme levels were not measured.

Mental confusion was reported in four of Lewis's cases and is a common feature of severe hepatic failure.[13] Confusion was noted in this case but high fever can itself produce this state in patients postoperatively and it cannot be ascribed solely to liver failure.

Obesity has been shown to influence the incidence of hepatic enzyme increases following exposure to halothane; enzyme levels were elevated in 48% of obese patients but in only 10% of nonobese.[14] No such relationship could be detected for ethrane. Whilst genetic factors appear to be of some significance for halothane toxicity, neither clinical[15] nor laboratory[16] studies have found this to be true for enflurane.

The cause of this patient's death is obscure. Hepatic failure which leads to accumulation of metabolites and toxic intracellular products does not normally result in death as rapidly as this.[13] The patient had a history of myocardial infarction 5 years previously and this was confirmed by the postmortem findings. She was also found to have aortic sclerosis. Ventricular tachydysrhythmia induced by fever and myocardial ischaemia, may have been the terminal event. As continuous ECG monitoring was not employed, this must remain speculative. Nevertheless, we consider this case to show an early stage of the hepatotoxic change induced by enflurane.

The pathogenesis of liver injury following enflurane exposure in the human is still unclear. Animal models generally require associated conditions of enzyme induction, starvation and hypoxia to a degree which makes their relevance to human studies very questionable.[17,18]

It seems likely that the relatively low incidence of severe hepatic damage attributable to enflurane is related to the fact that only 2–3% of enflurane undergoes biotransformation[19] compared with 15–20% of halothane.[20] The number of fatalities as a percentage of total cases reported is only 21% for enflurane,[11] but up to 50% in the case of halothane toxicity.[21] Evidence that favours idiosyncratic hypersensitivity as the principal mechanism of enflurane-induced hepatic damage, is strong. The frequency of prior exposure, fever and eosinophilia all point to a hypersensitivity mechanism.

Enzyme induction by drugs and by the volatile agents themselves is believed to enhance metabolic degradation of volatile agents, thereby generating toxic products which damage the liver directly or through a hypersensitivity mechanism.[21,22] Enflurane, unlike halothane and methoxyflurane, has not yet been shown to cause enzyme induction in man.

The effects of repeated enflurane exposure on liver function are controversial. Dundee *et al.*[14] showed that enzyme levels increased in almost 25% of patients who received enflurane on two to five occasions but Allen and Downing[23] failed to confirm this in a group of 49 women who received enflurane on up to three occasions. The available evidence suggests that enflurane is significantly less hepatotoxic than halothane and that the mortality of enflurane hepatotoxicity is also significantly less than that associated with halothane.

Conclusion

The clinical and histological evidence which implicates enflurane as the causative agent in this patient's massive hepatic destruction and death, is very strong. By a quirk of fate she may have been the first case of death from enflurane hepatitis, unreported until 10 years after her death.

Because crossreactivity does appear to exist between halothane and enflurane,[24] it would seem prudent to avoid repeat enflurane exposure in any patient who has demonstrated previous signs of toxicity or hypersensitivity (fever, eosinophilia or signs of liver damage) following the administration of either halothane or enflurane.

References

1. Van der Reis L, Askin SJ, Frecker GN, Fitzgerald WJ. Hepatic necrosis after enflurane anesthesia (letter). *Journal of the American Medical Association* 1974; **227**: 76.
2. Sadove MS, Kim SI. Hepatitis after use of two different fluorinated anesthetic agents. *Anesthesia and Analgesia* 1974; **53**: 336–40.
3. Denlinger JK, Lecky JH, Nahrwold ML. Hepatocellular dysfunction without jaundice after enflurane anesthesia. *Anesthesiology* 1974; **41**: 86–7.
4. Tsang HS. Jaundice after enflurane anesthesia. *Illinois Medical Journal* 1975; **148**: 593–4.
5. Ona FV, Patanella H, Ayub A. Hepatitis associated with enflurane anesthesia. *Anesthesia and Analgesia* 1980; **59**: 146–9.
6. Kline MM. Enflurane-associated hepatitis. *Gastroenterology* 1980; **79**: 126–7.
7. Danilewitz MD, Braude BM, Block HM, Botha J, Kew MC. Acute hepatitis following enflurane anaesthesia. *British Journal of Anaesthesia* 1980; **52**: 1151–3.
8. Spiegel RJ, Pizzo PA, Fantone JC, Zimmerman HJ. Fatal hepatic necrosis after high-dose chemotherapy following haloalkane anesthesia. *Cancer Treatment Reports* 1980; **64**: 1023–9.
9. White LB, DeTarnowsky GO, Mir JA, Layden TJ. Hepatotoxicity following enflurane anesthesia. *Digestive Diseases and Sciences* 1981; **26**: 466–9.
10. Douglas HJ, Eger EI II, Biava CG, Renzi C. Hepatic necrosis associated with viral infection after enflurane anesthesia. *New England Journal of Medicine* 1977; **296**: 553–5.
11. Lewis JH, Zimmerman HJ, Ishak KG, Mullick FG. Enflurane hepatotoxicity. A clinicopathological study of 24 cases. *Annals of Internal Medicine* 1983; **98**: 984–92.
12. Reynolds JEF, ed. *Martindale*. London: The Pharmaceutical Press, 1982: 257.
13. Eddleston ALWF. Acute hepatitis and fulminant hepatic failure. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Oxford: Oxford University Press, 1983: 12.195–12.203.
14. Dundee JW, Fee JPH, McIlroy PDA, Black GW. Prospective study of liver function following repeat halothane and enflurane. *Journal of the Royal Society of Medicine* 1981; **74**: 286–91.
15. Hoft RH, Bunker JP, Goodman HI, Gregory PB. Halothane hepatitis in three pairs of closely related women. *New England Journal of Medicine* 1981; **304**: 1023–4.
16. Gourlay GK, Adams JF, Cousins MJ, Hall P. Genetic differences in reductive metabolism and hepatotoxicity of halothane in three rat strains. *Anesthesiology* 1981; **55**: 96–103.
17. Lind RC, Gandolfi AJ, Sipes IG, Brown BR Jr. Comparison of the requirements for hepatic injury with halothane and enflurane in rats. *Anesthesia and Analgesia* 1985; **64**: 955–63.
18. Gelman S. Are the requirements for hepatic injury with halothane and enflurane in rats really different? (letter). *Anesthesia and Analgesia* 1986; **65**: 545–7.
19. Chase RE, Holoday DA, Fiserove-Bergerova V, Saidman LJ, Mack FE. The biotransformation of ethrane in man. *Anesthesiology* 1971; **35**: 262–7.
20. Cascorbi HF, Blake DA, Helrich M. Differences in the biotransformation of halothane in man. *Anesthesiology* 1970; **32**: 119–23.
21. Zimmerman HJ. *Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver*. New York: Appleton-Century-Crofts, 1978: 370–94.
22. Van Dyke RA. Biotransformation of volatile anaesthetics with special emphasis on the role of metabolism in the toxicity of anaesthetics. *Canadian Anaesthetists' Society Journal* 1973; **20**: 21–33.
23. Allen PJ, Downing JW. A prospective study of hepatocellular function after repeated exposures to halothane or enflurane in women undergoing radium therapy for cervical cancer. *British Journal of Anaesthesia* 1977; **49**: 1035–9.
24. Gottlieb LS, Trey C. The effects of fluorinated anesthetics on the liver and kidneys. *Annual Review of Medicine* 1974; **25**: 411–29.

Anaesthesia, 1987, Volume 42, pages 1197–1200

CASE REPORT

Retrograde intubation

Management of a 4.8-kg, 5-month infant

C. M. S. COOPER AND A. MURRAY-WILSON

Summary

An infant with Goldenhar's syndrome is presented in whom two-stage plastic surgery was undertaken. The first operation, at the age of 5 months, necessitated a retrograde technique for tracheal intubation while in the second, at 10 months of age, conventional intubation was possible. The discussion highlights those refinements that promote a successful outcome when retrograde intubation is indicated, particularly in infants.

Key words

Anaesthesia; paediatric.
Intubation, tracheal; technique.

Goldenhar's syndrome is a very rare congenital hemicraniofacial dysmorphology described in 1952.[1] Corrective surgery of facial and palatal abnormalities is often required during the first year. Difficult or impossible tracheal intubation should be anticipated.

Stehling[2] reported her experience with three cases of Goldenhar's syndrome. Each patient required three anaesthetics; one child needed tracheostomy on each occasion, one was moderately difficult to intubate and the third was intubated with ease. The facial appearance is not a reliable guide to difficulties with the airway. Vertebral anomalies may limit neck movement.

Case history

A 5-month-old male infant with the syndrome presented for repair of cleft lip and removal of accessory auricle. Further surgery to correct left-sided macrostomia and cleft palate was planned at 10 months of age. The child had been born at 34 weeks' gestation with multiple congenital abnormalities, that included an abnormal left ear, left microphthalmia and micrognathia. Heart failure shortly after birth, due to a ventricular septal defect complicated by a respiratory infection, was treated successfully with antibiotics, digoxin and frusemide; these were subsequently discontinued.

Physical examination revealed a 4.8-kg male with marked micrognathia, left macrostomia, a maximum intergingival opening of approximately 20 mm, unrestricted movement of head and neck, midline trachea and a good airway both at rest and while crying. Auscultation of the chest was normal apart from a systolic murmur.

Anaesthetic technique

Premedication was restricted to atropine 0.1 mg intramuscularly. Preparations for a difficult

---

C.M.S. Cooper, BSc, MB, BS, Registrar, A. Murray-Wilson, FFARCS, Consultant, Sheffield Children's Hospital.
Correspondence should be addressed to Dr C.M.S. Cooper, Department of Anaesthesia, Medical School, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2RX.

0003–2409/87/111197 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

intubation included the facility for retrograde intubation and the surgeon was briefed on the possible need for immediate tracheostomy. Anaesthesia was induced with halothane and nitrous oxide in 50% oxygen and maintained with halothane in 100% oxygen. Free spontaneous breathing was maintained with the aid of positive end expiratory pressure applied by partly obstructing the tail of the bag of a modified Ayre's T-piece system. A vein was cannulated and prophylactic antibiotics administered.

Five attempts at visualisation of the larynx and blind oral and blind nasal intubation of the trachea were unsuccessful; on one occasion two laryngoscope blades were used to gain more control of the tongue. These attempts revealed no view even of the epiglottis. A small folded towel was placed beneath the shoulders and the cricothyroid area was identified and cleaned. A short mid-line skin incision was made and an 18-gauge needle passed into the trachea in a slightly cephalad direction until a distinct 'pop' was elicited. The position was confirmed by easy aspiration of gas. The needle was angled to 45°, the position again confirmed and a 25-gauge, 30-cm polyvinylchloride catheter with introducing wire was passed through the needle. The catheter tip emerged from the left nostril and the needle was removed from the patient over the catheter. The catheter was moved down into the mouth via the complete palatal cleft and a lubricated Vygon 2.5-mm internal diameter tracheal tube passed over the catheter, which was now held taut, until resistance was met. The catheter was withdrawn completely but the tracheal tube could be advanced no further; it merely buckled at the back of the tongue under any pressure. The tracheal tube was removed and the airway re-established with the mask. The procedure was repeated.

With the catheter once again in place and held taut, a more rigid Portex 2.5-mm tracheal tube was passed over it until resistance was met. Breath sounds were heard through the tracheal tube when the catheter was removed but again it could not be advanced. The 25-gauge catheter was passed into the proximal end of the tracheal tube to a distance calculated to be 25 mm beyond the distal tracheal tube tip. By rotation anticlockwise through 90°, the tracheal tube was passed with ease into the trachea over the catheter, which was then withdrawn. The correct position of the tracheal tube was confirmed and it was secured. Anaesthesia was maintained uneventfully. No signs of haemorrhage, haematoma formation or surgical emphysema appeared. Extubation was performed after reversal of relaxant drugs, with the child vigorous and awake. There were no postoperative problems.

A second operation was performed at 10 months of age. On examination, the child was 1.4 kg heavier, the micrognathia appeared slightly less pronounced, the cleft lip repair was healthy and the remaining features were unaltered. Preparation for, and induction of, anaesthesia were as before.

On this occasion, blind orotracheal intubation was achieved at the third attempt, with a Portex 3.0-mm tube. Anaesthesia and reversal were uneventful; the child maintained a good airway following extubation. The postoperative course was uncomplicated. Since then the child has been listed as a day case in another specialty at an adult hospital where the previous notes were not available!

Discussion

For our patient's first operation conventional intubation of the trachea proved impossible but it was realised that corrective surgery was highly desirable. In these circumstances the recommended possibilities in adults and older children include awake intubation, intubation using a fibreoptic laryngoscope, retrograde intubation and tracheostomy.

The term 'retrograde' intubation refers to a technique in which a guide is passed into the trachea and thence into the mouth or nose. A tracheal tube is then passed down over the guide until it enters the trachea. This technique was reported in 1960[3] and its use in adults and children has been reviewed recently with many alternative refinements tabulated.[4]

The age and size of the child made awake intubation inadvisable and, judging by the subsequent difficulties under anaesthesia, probably impossible. Fibreoptic intubation is limited to tracheal tubes of at least 4.5–5.0 mm internal diameter and requires considerable experience before it is used in difficult cases. Tracheostomy in this age group, particularly in the absence of a tracheal tube, carries many risks, requires considerable skill and is best suited to situations in which prolonged intubation is anticipated.

A retrograde method was used successfully in an 11.6-kg, 30-month child.[5] We found that this technique proved to be a rapid and straightforward method of tracheal intubation. The experience gained on this one occasion from an uncommon manoeuvre, has made us very aware of many fine points of detail. The following are of particular importance.

The technique should be considered in advance, and all the equipment must be to hand. A pre-operative throat swab should be sent for culture to define the local bacterial flora in case of ensuing neck wound or operation site infection. Palpation of the trachea and cricothyroid area suggests that the trachea is quite superficial but cannulation of the lumen is surprisingly difficult. Care is required to find the midline, to avoid adjacent structures and not to penetrate too deeply.

The best type and size of guide varies with each patient.[4] A flexible-tipped Seldinger wire is rigid enough to follow the internal anatomy and emerge nasally, and easily supports the tracheal tube which is passed over the wire. If oral intubation is required, a more flexible introducer, such as an epidural catheter, may be an advantage since it is easier to retrieve from the pharynx. Use of a floppy catheter for nasal intubation is time-consuming because a second guide requires to be passed nasally into the pharynx. The ends of both are retrieved, tied together and then pulled out through the nose. A floppy catheter with the introducing wire withdrawn a short distance, combines many of the advantages of the floppy catheter and the Seldinger wire.

In our case the situation was eased by the complete palatal cleft through which the guide was moved from the nose to the mouth. It would be best to have all three types of guide to hand. As with all catheter-inside-needle techniques, the needle should be removed when the guide has been passed; the catheter is never withdrawn through the needle.

The guide, once sited, should be held taut so as to aid passage of the tracheal tube. Any resistance to advancement of the tracheal tube may be due to its failure to enter the larynx. The short distance between the glottic opening and the point of entry of the guide into the trachea, has led some authors to recommend that the guide be passed through a Murphy Eye cut near the tracheal tube tip. Thus, when the tracheal tube stops advancing when the guide entry point is reached, a longer portion of it may be in the trachea.[4,5] However, we consider that use of the Murphy Eye in this way might allow the tip to be angled across the glottic opening and thereby create the risk that the tip misses the larynx. A Murphy Eye may encourage the accumulation of dried obstructive secretions at the tracheal tube tip when small tracheal tubes are used.[6]

Many authors recommend that another guide be passed down the tracheal tube if resistance is still encountered once the retrograde guide has been removed ,[4] or even before its removal. This case confirms the value of such a technique. It may be wise to pass the second guide before removal of the retrograde guide.

Tracheal tubes for patients of this size vary in rigidity. We found that a stiffer tracheal tube was easier to pass.

Other potential problems are laryngeal spasm, airway oedema, haemorrhage, haematoma formation and surgical emphysema. These have been reported as minor and infrequent sequelae in older children and adults[4] but would be of relatively more significance in small infants. We did not observe any of these problems, nor were they reported by Borland *et al.*[5] Adequate depth of anaesthesia is obviously a requirement if laryngeal spasm is to be avoided, and multiple attempts at intubation are likely to increase the risk of trauma. We confirmed an air leak prior to extubation of the trachea, and extubation was performed only when the child was vigorous, awake and showed signs of good spontaneous ventilation. Borland *et al.*[5] waited overnight before a guide was passed through the tracheal tube prior to extubation, in case re-intubation was required. This method may require anaesthesia to reduce tracheal, and carinal, stimulation.

On occasion, growth of the infant improves the likelihood of conventional intubation, as occurred in this case. However, early surgery is important to establish normal phonation. In addition, our patient had feeding difficulties even with a prosthesis and it was felt that early surgery warranted the risks of anaesthesia despite the possible difficulties. These difficulties were considerably reduced by the use of a retrograde technique for intubation.

Retrograde intubation in infants has been described as dangerous,[7] a comment made without supporting evidence but based perhaps on ex-

Anaesthesia, 1987, Volume 42, pages 1201–1203

CASE REPORT

Spinal cord compression during chronic epidural morphine administration in a cancer patient

D. VAN DIEJEN, J. J. DRIESSEN AND J. H. A. M. KAANDERS

Summary

A case is described of thoracic spinal cord compression that occurred during continuous epidural administration of morphine. Sensory loss and motor weakness in the legs disappeared after catheter removal and antibiotic treatment.

Key words

Anaesthetic techniques, regional; epidural.
Complications; infection.

Since the early 1980s chronic epidural administration of opioids has proven a valuable method of providing analgesia in selected patients with cancer.[1,2] Severe infectious complications in association with this method are very rare.[1–3] We report here a woman with cancer pain who developed reversible neurological symptoms due to thoracic spinal cord compression during continuous administration of morphine via an implanted polyurethane catheter with a subcutaneous access port.

Case history

In 1984 a 38-year-old woman underwent a right maxillectomy because of a poorly differentiated squamous cell carcinoma of the maxillary sinus. One year later she had developed several metastases in both lungs. Since early 1986 she complained of pain between the shoulder blades and in the right shoulder. Routine X rays of the region showed no abnormalities but a body scan showed a 'hot spot' in the second thoracic vertebra. Oral medication with paracetamol, indomethacin and nicomorphine in appropriate doses did not sufficiently relieve her pain and the side effects (nausea, drowsiness and constipation) of these drugs were considerable. After deliberation with the referring department of radiotherapy, it was decided to attempt to relieve her pain with epidural morphine. Because of her expected long survival, a polyurethane epidural catheter with a subcutaneous access port under the left breast was inserted on 11 July 1986. Localisation of the catheter tip at the level of the fourth thoracic vertebra was confirmed radiologically.

Morphine 10 mg/24 hours was delivered continuously with an external pump and complete pain relief was achieved. The wounds of the implanted catheter healed satisfactorily.

Four weeks after the implantation, the patient complained of pain, swelling and redness at the site of the implanted catheter. Administration of morphine was discontinued, cephalexin 1 g 6-

---

D. van Diejen, MD, J.J. Driessen, MD, PhD, Staff Members, Department of Anaesthesiology, J.H.A.M. Kaanders, MD, Resident, Department of Radiotherapy, St Radboud Hospital, Catholic University, Geert Groote Plein Zuid 10, 6500 HB Nijmegen, The Netherlands.

0003–2409/87/111201 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

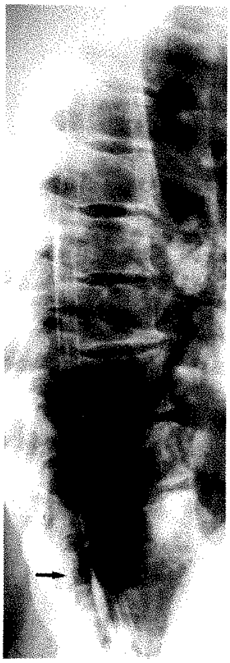


Fig. 1. Thoracic myelography. The lateral view shows a dorsal compression of the thecal sac from T_2 to T_{10}.

hourly commenced and the pain treated with oral nicomorphine and indomethacin. Two days later, when she rose from her bed, she experienced some weakness of the legs and numbness of the feet with new pains in the back and legs. She was admitted to hospital with manifest purulent infection of the area around the access port. The epidural catheter and subcutaneous port were removed and the consulted neurologist confirmed the suspicion of a threatening paraplegia. Clinical examination revealed slight paresis of both lower limbs and decreased sensation to pinprick in all dermatomes from T_{10} to S_5. A urinary catheter was inserted because of incontinence. A myelogram showed a dorsal compression of the spinal cord between the second and tenth thoracic vertebrae (Fig. 1).

An explorative mid-thoracic laminectomy was therefore performed. This showed an extensive, nonpurulent, firm epidural mass which could not be removed without risk of damage to the spinal cord. With the peroperative clinical suspicion of epidural metastasis, only a surgical biopsy was taken for microscopy and culture.

Postoperatively she was treated with intravenous cefuroxime 1 g 6-hourly for 2 weeks. The neurological deficit improved slowly and, some 4 weeks after the operation, she was discharged with only slight numbness of the soles of the feet.

Culture of the epidural biopsy showed no growth of microorganisms, while the culture of the access port of the catheter showed growth of *Staphylococcus aureus*. Microscopic examination of the epidural biopsy revealed fat and connective tissue together with extensive leucocytosis indicative of acute inflammation. There was no evidence of malignancy. Her pain was further relieved with indomethacin and nicomorphine.

Discussion

Chronic epidural administration of morphine in cancer patients causes surprisingly few infectious complications.[1-3] Zenz[2] noted two cases of reversible spinal infections in a larger series of 92 cancer patients on long-term treatment with intermittent administration of epidural morphine. Crawford *et al.*[3] reported one catheter tip culture of *Staphylococcus aureus* among 94 cancer patients, with concomittant septicaemia but without symptoms of infection around the spinal cord.

The proven bacterial infection of the subcutaneous pocket around the catheter suggests contamination of the epidural space in the patient presented here. The regression of the neurological deficits after removal of the epidural catheter and port, also suggests epidural infection. However, culture of the epidural biopsy remained negative and there was no pus in the epidural space. Treatment with cephalexin during the previous 4 days may have been the reason for this. Positive cultures (*Staphylococcus aureus*) were obtained and the presence of pus was demonstrated[4,5] in other reported cases of epidural abscesses or spondylitis during epidural drug administration.

Recent studies in animals and man have shown that chronically implanted epidural catheters can cause a fibrous reaction in the epidural space with thickening of the dura and with areas of apparent spinal cord compression.[1,6] A severe form of this type of sterile fibrotic inflammation of the dura and epidural space cannot, therefore, be excluded in our patient. Neurological deficits due to either epidural abscess or sterile epidural inflammation, although very rare, may complicate chronic epidural administration of opioids in cancer patients. Therefore, strict aseptic techniques should be used in these patients. Further investigation of the histopathological changes due to catheter material and drugs in the long-term epidural administration of opioids is necessary.

Acknowledgments

The authors thank Dr J. Merx of the Department of Radiology for his contribution and Mrs W. de Bont-Arens for preparing this manuscript.

References

1. Coombs DW. New approaches to chronic pain therapy. In: Katz RL, ed. *Seminars in anaesthesia, Vol. IV. Pain, Part II.* New York: Grune and Stratton, Inc., 1985: 287–99.
2. Zenz M. Epidural opiates for the treatment of cancer pain. In: Zimmerman M, Drings P, Wagner G, eds. *Recent results in cancer research, Vol. 89. Pain in the cancer patient.* Berlin: Springer Verlag, 1984: 107–15.
3. Crawford ME, Andersen HB, Augustenborg G, Bay J, Beck O, Benveniste D, Larsen LB, Carl P, Djernes M, Eriksen J, Greel AM, Henriksen H, Johansen SH, Jorgensen HO, Moller IW, Pedersen JE, Ravlo O. Pain treatment on outpatient basis utilizing extradural opiates. A Danish multicentre study comprising 105 patients. *Pain* 1985; **16:** 41–7.
4. North JB, Brophy BP. Epidural abscess: a hazard of spinal epidural anaesthesia. *Australian New Zealand Journal of Surgery* 1979; **49:** 484–5.
5. Wenningsted-Torgard K, Heyn J, Willumsen L. Spondylitis following epidural morphine. A case report. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 649–51.
6. Edwards T, Burney RG, Cappadona D, de Girolami U. Histopathologic changes induced in the epidural space and central neural elements of the guinea pig during chronic epidural morphine administration. *Regional Anesthesia* 1985; **10:** 45–6 (Abstract).

Anaesthesia, 1987, Volume 42, pages 1204–1206

CASE REPORT

Large dose epidural sufentanil

Management of postoperative pain with few side effects

T. H. MADEJ, N. C. WATSON AND B. C. MARTIN

Summary

The postoperative analgesic management of a patient who was intolerant of morphine and pethidine is described. An epidural infusion of fentanyl up to 1 μg/kg/hour was ineffective for analgesia in the first 18 hours. Subsequently, 50-μg boluses and an infusion of 0.5 μg/kg/hour sufentanil provided satisfactory analgesia with minimal side effects for 28 hours.

Key words

Anaesthetic techniques, regional; epidural.
Analgesics, narcotic; fentanyl, sufentanil.

Epidural administration of the new opioid agonist, sufentanil, may be provided by a single bolus injection,[1] when it has a rapid onset of action; a dose of 50 μg gives analgesia for 2–6 hours.[1,2] The combination of high lipid solubility[3] and high affinity for the mu-opioid receptor[4] makes sufentanil an appropriate drug, with the prospect of segmental analgesia and few central side effects. We present a patient with unusually high analgesic demands in whom epidural injection and infusion of sufentanil provided satisfactory postoperative analgesia with negligible morbidity.

Case history

A 41-year-old, 50-kg Caucasian woman with the diagnosis of loin pain haematuria syndrome was admitted for autotransplantation of her left kidney.[5] This syndrome describes the association of recurrent renal pain, haematuria and abnormalities of the intrarenal vasculature. She had previously had a right nephrectomy for loin pain and, on this occasion, ethical committee approval was granted for autotransplantation to denervate the remaining kidney. At home she received oral pethidine 125–200 mg every 4 hours for pain. On admission to hospital she received intramuscular pethidine 100–200 mg up to 3-hourly. The following day she suffered a grand mal seizure 20 minutes after the intramuscular administration of 200 mg pethidine and 50 mg dimenhydrinate. A total of 1550 mg intramuscular pethidine had been given in the preceding 24 hours. Sixty-two hours later, a second seizure occurred 10 minutes after a further dose of 200 mg pethidine; during this period she had received a further 2900 mg of pethidine. The analgesic prescription was reduced to a maximum of 100 mg pethidine 3-hourly. Over the next 4 days she received 3330 mg pethidine but felt that her pain relief was inadequate.

T.H. Madej, BM, BCh, FFARCS, Lecturer, N.C. Watson, FRCP(C), Consultant, B.C. Martin, BM, Resident Anaesthetist, Department of Anaesthesia, Foothills Hospital at the University of Calgary, 1403 29th Street NW, Calgary, Alberta T2N 2T9, Canada.
Correspondence should be addressed to Dr N.C. Watson please.

0003–2409/87/111204 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

The provision of adequate postoperative pain relief was thought to be unlikely with pethidine. Morphine was ruled out since she had suffered a pruritic maculopapular rash and dyspnoea with previous administration. Epidural fentanyl was therefore selected as the technique of choice for post-transplant analgesia. An epidural catheter was placed at T_{11}–T_{12} after induction of general anaesthesia. A bolus of fentanyl 100 μg was given, followed by an infusion of 30 μg/hour (10 μg/ml) through the epidural catheter. The infusion was continued postoperatively for 14 hours but was inadequate and required supplementation with intramuscular pethidine 75 mg on two occasions. A bolus of fentanyl 100 μg and an increase of the epidural infusion to 50 μg/hour for 4 hours did not significantly improve analgesia, although the patient was drowsy at this dose. The decision was made to try a different analgesic.

Sufentanil 50 μg (5 μg/ml) as a single bolus epidural injection provided analgesia for 2–3 hours. After two more bolus doses, an epidural infusion of sufentanil 15 μg/hour was started. This was increased to 20 μg/hour after 3 hours and again to 25 μg/hour after 6 hours. At 25 μg/hour the patient appeared comfortable. After 5 hours at this dose, the infusion was gradually decreased to zero over the next 4 hours; analgesia was then successfully provided by intramuscular pethidine.

During the sufentanil infusion the patient's end tidal carbon dioxide was monitored continuously using a capnograph and nasal catheter[6] for 18 hours from commencement of the sufentanil infusion. Initially the end tidal carbon dioxide was 6.5 kPa and did not increase above this over the next 18 hours but fluctuated between 4.0 and 6.2 kPa. The patient's respiratory rate did not decrease below 10 breaths/minute and no episodes of apnoea were recorded. Anti-emetic prophylaxis was not given and the patient was nauseated only on one occasion, when a bolus of sufentanil was given rapidly. The patient suffered no pruritus but was drowsy when she received 25 μg/hour.

Discussion

This patient's high analgesic requirements gave rise to problems both pre- and postoperatively. Thorough investigation, including a CAT scan, failed to reveal any cause for the pre-operative convulsion other than large and repeated doses of pethidine,[7] causing an accumulation of normeperidine despite normal renal and hepatic function.[8]

Fentanyl as a continuous epidural infusion has provided satisfactory results[9] and gives more effective postoperative analgesia than a conventional intramuscular regimen.[10] However, our patient did not have pain relief after fentanyl 1 μg/kg/hour epidurally. The dose of the fentanyl infusion was not increased, since the patient was drowsy and 1 μg/kg/hour is the maximum dose which has been used in this hospital[6] and in other studies.[9,10]

Sufentanil has a number of potential advantages compared to fentanyl for epidural use. The higher affinity of sufentanil for the mu-opiate receptor[4] and greater potency[11] reduce the risk of CNS-mediated side effects. A study in rats demonstrated preferential binding of mu-opiate receptors in the spinal cord and fewer CNS-mediated side effects following epidural, as compared with intravenous, administration of sufentanil.[12] The relative potency of sufentanil and fentanyl in the epidural space in humans is unknown. Drug potencies cannot be compared in this case, since the degree of pain diminished with time and equivalent analgesia was not obtained. In cats and rats, intrathecal sufentanil is more potent than fentanyl and has a longer duration at equi-analgesic doses.[3,13] High concentrations of sufentanil intrathecally do not give rise to the hyperaesthesia observed at comparable concentrations of morphine in cats and rats.[14] The smaller volume of distribution and shorter terminal half-life of sufentanil, compared to fentanyl, reduce the risk of systemic accumulation with repeated doses or infusions.[11] This patient suffered few side effects from the epidural infusion of either fentanyl or sufentanil. She was satisfied with the quality of analgesia for only 2 hours after each of the three bolus doses of sufentanil 50 μg and for 5 hours while she received 25 μg/hour by infusion.

In conclusion, the infusion of sufentanil epidurally provided adequate analgesia in a patient with high analgesic requirements. Continuous monitoring of end tidal carbon dioxide enabled the dose to be increased safely and, even at an epidural sufentanil infusion rate of 0.5 μg/kg/hour, respiratory depression was not observed.

References

1. Donadoni R, Rolly G, Noorduin H, Vanden Bussche G. Epidural sufentanil for postoperative pain relief. *Anaesthesia* 1985; **40:** 634–8.
2. Tan S, Cohen SE, White PF. Sufentanil for analgesia after cesarean section: intravenous versus epidural administration. *Anesthesia and Analgesia* 1986; **65:** S158.
3. Yaksh TL, Noueihed RY, Durant PAC. Studies of the pharmacology and pathology of intrathecally administered 4-anilinopiperidine analogues and morphine in the rat and cat. *Anesthesiology* 1986; **64:** 54–66.
4. Leysen JE, Gommeren W, Niemegeers CJE. [^{3}H]-Sufentanil, a superior ligand for μ-opiate receptors: binding properties and regional distribution in rat brain and spinal cord. *European Journal of Pharmacology* 1983; **87:** 209–25.
5. Sheil AGR, Ibels LS, Thomas MAB, Graham JC. Renal autotransplantation for severe loin-pain/haematuria syndrome. *Lancet* 1985; **2:** 1216–7.
6. Ahuja BR, Strunin L. Respiratory effects of epidural fentanyl. *Anaesthesia* 1985; **40:** 949–55.
7. Jaffe JH, Martin WR. Opioid analgesics and antagonists. In: Gilman AG, Goodman LS, Rall TW, Murad F, eds. *The pharmacological basis of therapeutics.* New York: Macmillan, 1985: 151.
8. Kaiko RF, Foley KM, Grabinski PY, Heidrich G, Rogers AG, Inturrisi CE, Reidenberg MM. Central nervous system excitatory effects of meperidine in cancer patients. *Annals of Neurology* 1983; **13:** 180–5.
9. Bailey PW, Smith BE. Continuous epidural infusion of fentanyl for postoperative analgesia. *Anaesthesia* 1980; **35:** 1002–6.
10. Welchew EA, Thornton JA. Continuous thoracic epidural fentanyl. A comparison of epidural fentanyl with intramuscular papaveretum for postoperative pain. *Anaesthesia* 1982; **37:** 309–16.
11. Rosow CE. Sufentanil citrate: a new opioid analgesic for use in anesthesia. *Pharmacotherapy* 1984; **4:** 11–19.
12. Colpaert FC, Leysen JE, Michiels M, van den Hoogen RHWM. Epidural and intravenous sufentanil in the rat: analgesia, opiate receptor binding, and drug concentrations in plasma and brain. *Anesthesiology* 1986; **65:** 41–9.
13. Aoki M, Senami M, Kitahata LM, Collins JG. Spinal sufentanil effects on spinal pain-transmission neurons in cats. *Anesthesiology* 1986; **64:** 225–9.
14. Yaksh TL, Harty GJ, Onofrio BM. High doses of spinal morphine produce a nonopiate receptor mediated hyperesthesia: clinical and theoretical implications. *Anesthesiology* 1986; **64:** 590–7.

Anaesthesia, 1987, Volume 42, pages 1207–1208

CASE REPORT

Bradycardia during elevation of zygomatic fractures

A variation of the oculocardiac reflex

E. S. SHEARER AND R. WENSTONE

Summary

Two cases of severe bradycardia are described which occurred during elevations of zygomatic fractures. The two patients and the possible mechanisms involved are discussed.

Key words

Complications; bradycardia.
Surgery; faciomaxillary.

The oculocardiac reflex is a phenomenon well known to anaesthetists engaged in ophthalmic work. We report two cases that demonstrated what we believe to be a hitherto unreported variation of this reflex: that elicited by elevation of zygomatic fractures.

Case histories

Case 1

This was a healthy, 43-year-old man who weighed 79 kg and had sustained a depressed left zygomatic fracture in an affray 5 days prior to hospital admission. He was medically fit, had no previous anaesthetic history and was unpremedicated. Anaesthesia was induced with thiopentone 425 mg followed by suxamethonium 75 mg. The trachea was intubated with an oral 9.5-mm cuffed tracheal tube. On return of some movement, atracurium 0.5 mg/kg was given and anaesthesia maintained with 0.5% halothane and 66% nitrous oxide in oxygen (fresh gas flow 6 litres/minute) using a Manley Servovent ventilator. Monitoring was by means of an ECG and oscillotonometer.

Surgery proceeded uneventfully with the systolic blood pressure (BP) maintained at 120 mmHg and pulse at 80 beats/minute in sinus rhythm. The pulse decreased to 60 beats/minute (sinus rhythm) at the first attempt to elevate the fracture and recovered to 80 beats/minute immediately on cessation of the stimulus. The second and successful attempt to elevate the fracture caused the pulse to decrease to 30 beats/minute with a junctional rhythm and then to sinus arrest for 4 seconds. This reverted spontaneously to a junctional rhythm at 30 beats/minute. Intravenous atropine 600 μg converted this to a sinus tachycardia of 120 beats/minute with frequent ventricular ectopics. This gave way to a bigeminal rhythm which itself reverted spontaneously to a sinus tachycardia. This whole episode lasted one minute. The rest of anaesthesia was uneventful. Reversal of residual neuromuscular blockade was with neostigmine 2.5 mg and glycopyrronium 0.5 mg. A postoperative ECG was normal.

E.S. Shearer, MB, ChB, DA, Registrar, R. Wenstone, MB, ChB, DA, Senior House Officer, Department of Anaesthesia, Walton Hospital, Rice Lane, Liverpool L9 1AE.

0003–2409/87/111207 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Case 2

This was an 18-year-old man who presented with a left zygomatic fracture also following an affray. He was medically fit and weighed 65 kg. His only previous general anaesthetic was for an uneventful appendicectomy. He presented and was anaesthetised 3 days after the injury.

He was premedicated with oral diazepam 10 mg, 90 minutes pre-operatively. Anaesthesia was induced with fentanyl 100 μg and thiopentone 300 mg. Atracurium 0.5 mg/kg was then given. The patient's trachea was intubated with a 9.5-mm cuffed orotracheal tube and anaesthesia maintained with 0.8% enflurane and 66% nitrous oxide in oxygen. Ventilation was assisted using a Manley Servovent with a circle system (fresh gas flow 6 litres/minute). The patient was monitored with an ECG and oscillotonometer.

Again, initial surgery was uneventful. Systolic blood pressure and pulse rate were both stable at 120 mmHg and 70 beats/minute, respectively. However, the pulse decreased to 30 beats/minute as soon as an attempt was made to elevate the fracture. The ECG showed a junctional rhythm. Systolic blood pressure was 100 mmHg. The pulse recovered as soon as the stimulus ceased but it was 4 minutes before it reached 70 beats/minute again. His blood pressure remained at 100 mmHg during this period.

The remainder of anaesthesia was uneventful. Neuromuscular blockade was reversed with neostigmine 2.5 mg and atropine 1.2 mg.

Discussion

Bradycardia associated with traction on the eye was first noted by Aschner[1] and Dagnini[2] in 1908 and has since been well documented to occur with many stimuli in and around the orbit as well as with facial fractures that involve the mid-face.[3] The reflex has remained an important, even if predictable, problem to anaesthetists involved in ophthalmic work.

Our cases are the first to describe a reflex bradycardia similar to the oculocardiac reflex, but that occurred with stimuli which did not directly involve the orbit, since there was no direct surgical manipulation of the eye nor was there any traction on a fracture line passing through the orbit.[3]

The anatomical pathway of the classical oculocardiac reflex is well known: the afferent limb is carried by parasympathetic fibres in the trigeminal nerve passing via the ciliary nerves, ciliary ganglion and nasociliary nerves. The efferent limb is provided by the vagus nerve. The pathway which the reflex we describe follows is less obvious in regard to the afferent limb. We wonder whether it may be from parasympathetic fibres that supply the periosteum of the zygoma. We initially considered that inadvertent pressure on the eye by the surgeons' fingers during elevation of the fracture could be the cause of the bradycardia, but we were careful to ensure that this did not occur.

Since reporting these two cases we have noticed bradycardias of varying severity in many more cases of elevations of zygoma, always just as elevation is attempted. Indeed, this reflex appears to be elicited so easily that we now routinely give these patients atropine at induction of anaesthesia. It is interesting to speculate why such an apparently common reflex in such a common procedure has not been reported before. One possibility is that, as the majority of these patients are generally fit and healthy, the routine monitoring may not always include an ECG and/or pulse monitor.

It is our opinion, highlighted by these two cases, that the possibility of a reflex bradycardia during elevation of zygomatic fractures should always be anticipated, that a suitable anticholinergic drug (e.g. atropine) should be instantly available and that all these patients should be monitored by means of an ECG or pulse monitor.

References

1. Aschner B. Über einen Bischer noch nicht beschreiben en Reflex vom Auge auf Kreislauf und Atmung: Verschwinden des Radialispulses bei Druck auf das Auge. *Wiener Klinische Wochenschrift* 1908; **21:** 1529–30.
2. Dagnini G. Intorno ad un riflesso provocato in alcuni emiplegici collo stimolo della corne e colla pressione sul bulbo oculare. *Bullettino delle Scienze Mediche della Societa Medica di Bologna* 1908; **8:** 380–1.
3. Robideaux V. Oculocardiac reflex caused by mid-face disimpaction. *Anesthesiology* 1978; **49:** 433.

Anaesthesia, 1987, Volume 42, pages 1209–1211

CASE REPORT

Upper airway obstruction in neurofibromatosis

W. C. CROZIER

Summary

A patient with von Recklinghausen's neurofibromatosis developed severe upper airway obstruction at the induction of anaesthesia and required emergency cricothyroidotomy. The cause was a neurofibroma at the base of the tongue. Features of von Recklinghausen's neurofibromatosis which may be of importance to the anaesthetist are reviewed.

Key words

Anatomy; airway.
Intubation, tracheal; difficulty.

Case history

A 24-year-old woman presented for operative stabilisation of a mandibular fracture that involved the mandibular symphisis and the left mandibular angle. The fracture had been sustained 20 hours previously after a fist blow. The patient had been diagnosed previously as having von Recklinghausen's neurofibromatosis (VRN), with multiple skin lesions on the chest and abdomen but no neurological or other symptoms. She had received general anaesthesia for Caesarean section on two occasions 4 years and 2 years previously, and no difficulty was reported. Physical examination revealed a mildly obese, emotionally distressed woman with asymmetrical swelling over the left parotid area, and mouth opening limited to approximately 2 cm because of pain. Her tongue appeared to be swollen and she was unable to articulate clearly but it was assumed that this was because of her fracture. A lateral neck X ray showed some submandibular swelling but a patent airway. History and examination were otherwise normal.

The patient had been starved for 20 hours. No bleeding had occurred for over 12 hours and none of her teeth were displaced. Following preoxygenation, anaesthesia was induced with thiopentone. Muscle relaxation was produced by suxamethonium after pretreatment with a small dose of pancuronium. Ventilation of her lungs was possible at this time with a mask and airway but her airway was partially obstructed and a tidal volume of only about 200 ml was achieved. Nasal intubation was attempted but this proved to be impossible. Her mouth opened adequately but direct laryngoscopy did not assist intubation since there was a large mass at the base of the tongue. Pulling the tongue forwards did not help. Manual ventilation became more difficult and her oxygen saturation (measured by a pulse oximeter) began to decrease precipitously. The problem did not appear to be due to laryngeal spasm but to a valve-like effect of the

---

W.C. Crozier, MB, BS, FFARCS, Visiting Assistant, Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Medical Institutions, N. Wolfe Street, Baltimore, Maryland 21205, USA.

0003–2409/87/111209 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

mass. The surgeon was asked to perform an emergency cricothyroidotomy. This was complicated by haemorrhage. Immediately before the tracheostomy tube was inserted, her oxygen saturation was 35% and she developed a bradycardia of 40 beats/minute with widened QRS complexes on the electrocardiogram. These changes resolved spontaneously within only a few seconds of administration of 100% oxygen through the tracheostomy tube and cardiovascular stability was regained rapidly. At no time were there changes in pupil size or reactivity. Subsequently, a formal tracheostomy was fashioned and the mass biopsied; mandibular stabilisation was accomplished without difficulty. The patient was stable at the end of the procedure. She was transferred to the intensive care unit where she awoke promptly. She sustained no neurological deficit and the ECG showed no injury pattern. Some right-sided lung changes were present both clinically and radiologically, probably as a result of bleeding during the cricothyroidotomy, but they did not cause disturbance of blood gases and they resolved rapidly.

Examination of the biopsy revealed that the mass was a plexiform neurofibroma. Most of the mass, which measured 5 × 5 × 3 cm, was removed by laser surgery one week after the initial operation. Subsequent questioning revealed a 2-year history of speech disturbance for which the patient had not sought medical advice.

Discussion

Von Recklinghausen's neurofibromatosis is a relatively common, genetically determined disease that occurs in between 1:2500 and 1:3300 live births.[1,2] The clinical features are so many and varied that a VRN patient who presents with one aspect of the disease must be suspected of harbouring some of the other manifestations. The most important of these to the anaesthetist are features that affect the head, neck and airway.

The first case of neurofibromatosis, described by Smith in 1849 (pre-dating von Recklinghausen), also presented with a 'walnut-sized' mass in the tongue.[3] Baden *et al.*[4] gave an historical appraisal of the oral manifestations of VRN. They estimated that 5% of VRN patients have an intra-oral manifestation of the disease but only 1% would be expected to have a discrete lesion of the tongue. Our patient may also have had macroglossia but this was difficult to differentiate from swelling due to the trauma, or from a mass effect of the lesion. It was not sufficiently pronounced to make us attempt anything other than a usual laryngoscopic approach.

Other manifestations of VRN of significance to the anaesthetist include deformity of the facial bones, with asymmetry, hypertrophy or atrophy, macrocephaly,[4–6] macroglossia[4–7] and parapharyngeal tumours, which arise from a branch of a cranial nerve and can be massive, affecting most of the cervical spine.[8] In addition, a laryngeal neurofibroma can occur very rarely; only 20 such tumours have been recorded.[9] Thyroid enlargement occurs as a benign feature in 4.5% of patients with VRN.[10] Associated features include sensitivity to neuromuscular blocking agents,[11] kyphoscoliosis[2] and phaeochromocytoma, which occurs in less than 1% of VRN patients but is still much more common than in the general population.[7,12] Sipple's syndrome, a very rare combination of bilateral phaeochromocytoma, medullary thyroid carcinoma and neurofibromatosis,[13] and fibrosing alveolitis, which occurs in up to 20% of VRN patients between the ages of 35 and 60 years,[14] are also found.

In conclusion, this case demonstrates how a presenting surgical problem may mask an underlying lesion resulting from a progressive disease. Even though previous anaesthesia is reported to have been uneventful, the presence of a progressive disease such as VRN should raise the anaesthetist's level of suspicion and significant lesions should be sought.

References

1. Crowe FW, Schull WJ, Neel JV. *Multiple neurofibromatosis. A clinical, pathological and genetic study*. Springfield, IL: Charles C. Thomas, 1956.
2. Riccardi VM. Neurofibromatosis: an overview and new directions in clinical investigations. *Advances in Neurology* 1981; **29**: 1–9.
3. Smith RW. *A treatise on the pathology, diagnosis and treatment of neuroma*. Dublin, 1849.
4. Baden E, Pierce HE, Jackson WF. Multiple neurofibromatosis with oral lesions; review of the literature and report of a case. *Oral Surgery* 1955; **8**: 263–80.
5. Holt GR. E.N.T. manifestations of Von Recklinghausen's disease. *Laryngoscope* 1978; **88**: 1617–32.
6. Weichert KA, Dine MS, Benton C, Silverman FN. Macrocranium and neurofibromatosis. *Radiology* 1973; **107**: 163–6.

7. Riccardi VM. Medical progress. Von Recklinghausen neurofibromatosis. *New England Journal of Medicine* 1981; **305:** 1617–27.
8. Kukreja HK, Changani DL, Joshi KC. Neurofibroma of the parapharyngeal space. *Journal of Laryngology and Otology* 1977; **91:** 809–12.
9. Chang-Lo N. Laryngeal involvement in Von Recklinghausen's disease: a case report and review of the literature. *Laryngoscope* 1977; **87:** 435–42.
10. Brasfield RD, Dasgupta TK. Von Recklinghausen's disease: a clinicopathological study. *Annals of Surgery* 1972; **175:** 86–104.
11. Fisher MM. Anaesthetic difficulties in neurofibromatosis. *Anaesthesia* 1975; **30:** 648–50.
12. Hope DG, Mulvihull JJ. Malignancy and neurofibromatosis. *Advances in Neurology* 1981; **29:** 33–56.
13. Schimke RN, Hartmann WH, Prout TE, Rimoin DL. Syndrome of bilateral pheochromocytoma, medullary thyroid carcinoma and multiple neuromas. A possible regulatory defect in the differentiation of chromaffin tissue. *New England Journal of Medicine* 1968; **279:** 1–7.
14. Sagel SS, Forrest JV, Askin FB. Interstitial lung disease in neurofibromatosis. *Southern Medical Journal* 1975; **68:** 647–9.

Anaesthesia, 1987, Volume 42, pages 1212–1217

APPARATUS

Feedback control of neuromuscular blockade

A simple system for infusion of atracurium

C. M. WAIT, V. A. GOAT AND C. E. BLOGG

Summary

A simple system for closed-loop control of neuromuscular blockade is described. It comprises a Datex Relaxograph, a small relay and a syringe pump. The equipment is commercially available and requires no complex custom-built electronics. Atracurium was infused in a semicontinuous manner to 11 patients who underwent general anaesthesia for a variety of surgical procedures. Neuromuscular blockade oscillated within a narrow range around the preset level. The mean rate of infusion of atracurium was 0.5 mg/kg/hour (SD 0.13). The mean recovery time was 25.5 minutes (SD 7.95).

Key words

Equipment; infusion pumps, nerve stimulators, electromyographs.
Neuromuscular relaxants; atracurium.

The new intermediate-duration muscle relaxants atracurium and vecuronium are suitable for administration by continuous infusion because of their short duration of action and lack of cumulation on repeated dosage.[1,2] However, because there is a wide interindividual variation in dose response and because dose requirements may also vary during a long procedure, infusion rates need to be adjusted repeatedly to maintain a given level of neuromuscular blockade. If this adjustment is performed automatically, the anaesthetist is freed to attend to other aspects of patient care.

There has recently been renewed interest in feedback control of neuromuscular blockade and the feasibility of automated control in the clinical situation has been established. In one study proportional control was used to control the infusion of pancuronium to patients.[3] The controller used was of the authors' own design and the problems cited included excessive time taken to set up the equipment, and electrical interference from mains and surgical diathermy. Others[4] employed a more simple on–off control. They also used the elicited compound electromyogram (EMG) and equipment made in their department. The device intermittently activated an infusion of vecuronium in response to the EMG signal. They obtained satisfactory control of neuromuscular blockade in all the patients studied and calculated mean infusion rates were similar to published data for true continuous infusion of vecuronium.

Recently there has been a preliminary report of a system in which a Datex Relaxograph (Vickers Medical, Basingstoke, Hampshire) activates an infusion of relaxant via a controlling box of electronics.[5] The authors stated that the device achieves stable control of neuromuscular blockade and that it is simple to use. The

---

C.M. Wait, BM, BCh, FFARCS, Registrar, V.A. Goat, MB, ChB, FFARCS, C.E. Blogg, MB, BS, FFARCS, Consultants, Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford OX2 6HE.

0003–2409/87/111212 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

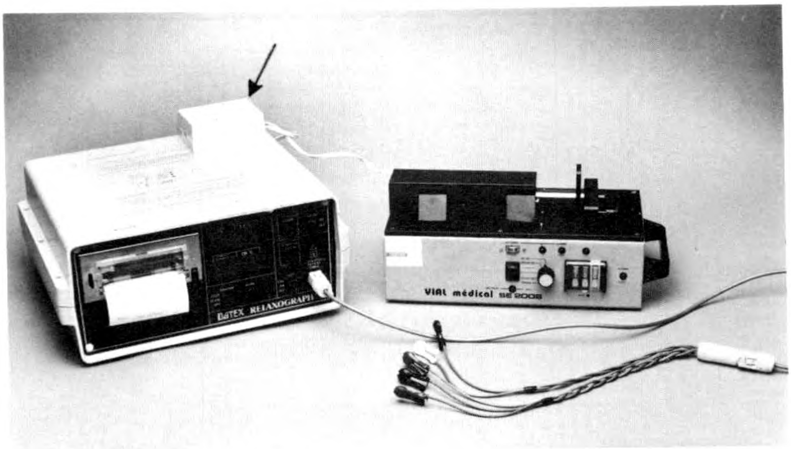


Fig. 1. The Relaxograph, syringe pump and interconnecting relay (arrowed).

objective of the current study was to establish whether the simple method of on–off control could be achieved in the clinical setting using commercially available equiment with minimal modification.

Apparatus

The system comprises a Relaxograph, a relay and a syringe pump modified to allow the relay to turn the pump on and off (Fig. 1). The Relaxograph is a compact electromyographic analyser which has recently been reviewed.[6] One feature of the device, the T_1 high alarm (not mentioned in the review), enables the Relaxograph to control the syringe pump without complex or expensive intervening electronics. The alarm can be set to trigger at any value of T_1 of the train-of-four from 0–100% of the reference value. When this threshold is exceeded the alarm is activated; a bleep sounds, a visual display flashes and a potential appears at the appropriate pin of the analogue output socket at the rear of the machine. When the value of T_1 falls below the same threshold the alarm switches off and the potential becomes zero again. We use this potential to switch a small relay which, when activated, completes a circuit to restore the low-voltage power supply to the syringe pump (Fig. 2). The relay is a simple reed device with a pull-in voltage of 5 volts (e.g. Archer 275-232, Tandy Corporation, Fort Worth, Texas). The pump is a Vial Medical 200B rechargeable battery device simply modified so that its on–off switch is interrupted by the (normally open) relay contacts.

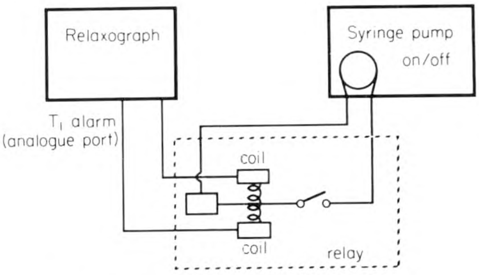


Fig. 2. Wiring diagram with details of the connexions between the components of the system.

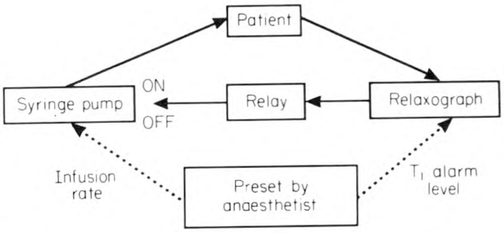


Fig. 3. Schematic diagram of closed-loop control system.

If the pump is primed with a suitable concentration of a neuromuscular blocking drug, the system functions as a closed-loop feedback system utilising on–off control (Fig. 3). Atracurium, an appropriate drug for administration by continuous infusion, was chosen to evaluate the system.

Patients and methods

Eleven adults were studied. All were ASA grade 2 or 3 and were scheduled for procedures of

Table 1. Patient details and anaesthetic technique.

Patient	Sex	Age, years	Weight, kg	Operation	Opiate	Volatile agent	Reversal
1	M	73	76	Aortic aneurysm	F	—	N G
2	M	72	86	Aortic aneurysm	F P	—	N G
3	M	57	71	Hemicolectomy	F	I	N A
4	F	76	66	Hip replacement	F	—	N G
5	F	47	59	Mastectomy	AF	I	N A
6	F	52	61	Hysterectomy	F	—	N A
7	M	41	79	Craniotomy	F	—	N A
8	F	43	66	Hysterectomy	F	I	N G
9	M	53	70	Renal transplant	F	I	N G
10	M	33	61	Renal transplant	SF	—	N G
11	M	46	70	Nephrolithotomy	F	I	N G
Mean (SD)		53.9 (14.2)	69.5 (8.25)				

For all patients anaesthesia was induced with thiopentone and maintained with nitrous oxide 70% in oxygen. F, Fentanyl; P, papaveretum; AF, alfentanil; SF, sufentanil; I, isoflurane; N, neostigmine; G, glycopyrronium; A, atropine.

intermediate to long duration which required muscle relaxation. Prior discussion with members of the local ethical committee established that formal ethical approval need not be sought. The non invasive method of neuromuscular monitoring and controlled administration of relaxant were felt to enhance patient safety. No particular constraints were placed upon the anaesthetic technique since the objective was to evaluate the control system in different clinical situations. Details of patients and anaesthesia are summarised in Table 1.

The Relaxograph stimulating electrodes were placed over the ulnar nerve at the wrist and the recording electrodes over the hypothenar eminence after the skin had been degreased with alcohol. The T_1 high alarm of the Relaxograph was set to the level of neuromuscular transmission that was required during the period of feedback control (e.g. 5%) and the audible alarm was muted.

Anaesthesia was induced with thiopentone 4–6 mg/kg and the patients' lungs inflated with nitrous oxide 70% in oxygen via a mask and Bain system with a fresh gas flow of 100 ml/kg/minute. The Relaxograph was then run through its calibration sequence (which normally takes less than 20 seconds) to establish a supramaximal stimulus and the 100% reference value for T_1. Atracurium 0.5 mg/kg was then administered through an indwelling cannula and the trachea was intubated. Anaesthesia was maintained with nitrous oxide 70% in oxygen, and an opiate. Analgesic supplements were given as clinically indicated and, in some cases, a volatile agent (isoflurane) was added. Ventilation was adjusted to maintain normocapnia if a capnograph was available or if invasive monitoring allowed arterial blood sampling.

In theatre, the syringe pump and syringe containing atracurium 5 mg/ml in 0.9% w/v saline were connected to the patient via a similarly primed catheter. This catheter joined a crystalloid infusion as close to the patient as possible. The pump was set to deliver atracurium at a rate of 1 mg/kg/hour. The feedback system was then activated before neuromuscular transmission had recovered to the level of T_1 that had been selected on the T_1 high alarm.

The feedback loop was inactivated 10–20 minutes before the anticipated end of the surgical procedure (depending on the nature of surgery and the anaesthetic technique) and recovery from neuromuscular blockade was allowed to proceed. Neostigmine 2.5 mg was administered with either atropine or glycopyrronium when T_1 had recovered to at least 25% of control. The trachea was extubated once clinically adequate neuromuscular transmission had returned as judged by satisfactory tidal volumes, sustained head lift and grip.

Neuromuscular monitoring was discontinued as soon as the patient was awake, to avoid possible discomfort from the Relaxograph stimulus. The neuromuscular data from the Relaxograph were collected and stored on disc by a BBC Model B microcomputer to facilitate subsequent analysis.

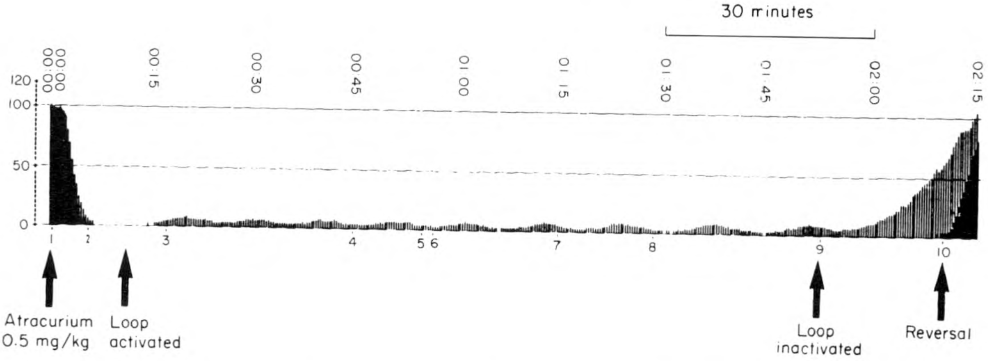


Fig. 4. Relaxograph printout which demonstrates feedback control of neuromuscular blockade (patient 3).

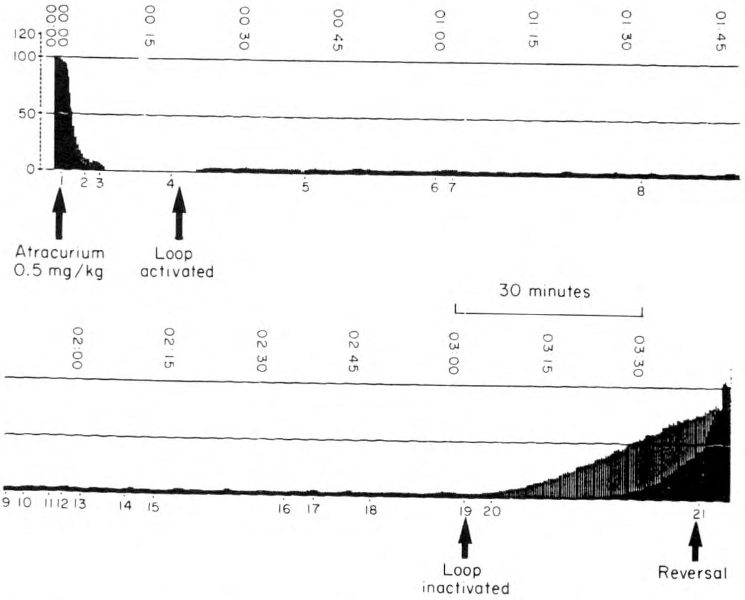


Fig. 5. Relaxograph printout which demonstrates feedback control of neuromuscular blockade (patient 10).

Results

The initial bolus dose of atracurium caused a lecrease in T_1 to zero in all but two patients numbers 2 and 10), who received a further 10 ng to facilitate intubation. In all patients, when ieuromuscular transmission had recovered to he preselected value of T_1 the syringe pump was utomatically activated and infused atracurium t a fixed rate until T_1 decreased below the same et point again, which stopped the infusion. The evel of blockade oscillated around the preset alue until the feedback loop was inactivated, whereupon spontaneous recovery commenced. Two representative Relaxograph recordings are shown in Figs 4 and 5.

Surgical relaxation was satisfactory in every case during the period of feedback control. The maximum deviation above the set point was 6% of the initial 100% value of T_1 (patient 4). The maximum deviation below the set point after recovery from the intubating dose was 3% of the 100% reference value ($T_{1,\text{ref}}$). In all but two patients (3 and 4) the amplitude of oscillation around the set point was 5% or less of $T_{1,\text{ref}}$ (Table 2).

Table 2. Closed-loop infusion data for atracurium.

Patient	Maximum deviation (percent $T_{1,ref}$) from set point during infusion*		Infusion duration, minutes	Total dose infused, mg	Mean rate of infusion, mg/kg/hour
	Above	Below			
1	2	3	77	31.6	0.32
2	2	3	70	55	0.55
3	5	2	96	63	0.56
4	6	3	53	25	0.43
5	2	2	25	10.3	0.42
6	1	2	31	19	0.60
7	2	2	188	122.1	0.49
8	3	1	20	10	0.45
9	1	1	156	57.5	0.32
10	2	1	157	100	0.62
11	3	2	39	35	0.77
Mean (SD)	3 (1.34)	2.36 (0.67)	82.9 (59.2)	48.0 (36.38)	0.50 (0.13)

* The set point is the level of the T_1 high alarm preset by the anaesthetist. This determines the level about which neuromuscular blockade oscillates during the period of feedback control. $T_{1,ref}$ refers to the 100% reference value of T_1 of the train-of-four obtained during calibration of the Relaxograph.

The mean duration of infusion, defined as the time from which the pump was first activated to the time the loop was disabled, was 82.9 minutes (range 20–188 minutes). The mean infusion rate, calculated by dividing the total dose of atracurium infused by the infusion duration, was 0.5 mg/kg/hour (SD 0.13).

Clinical recovery time, taken from the time the loop was disabled to the time of extubation, ranged from 16–40 minutes with a mean of 25.5 minutes (SD 7.95). No patient showed signs of clinically inadequate reversal at this time.

Discussion

We have devised an inexpensive system which unites the Relaxograph and syringe pump. An existing feature of the Relaxograph (the T_1 high alarm) is used in a novel way so that no complex custom-made electronics are required. Consequently, the technique is available to any anaesthetist who has the use of a Relaxograph and syringe pump.

This study confirms that the simple technique of on–off feedback control using atracurium can maintain stable levels of neuromuscular blockade in clinical practice. The mean infusion rate and relatively wide interpatient variation are similar to published data for continuous infusion of atracurium during balanced anaesthesia.[7]

The oscillations in the level of blockade are inherent to this type of control system but were not of a magnitude to be of clinical significance. The amplitude of oscillation can be reduced by attention to detail. Oscillation was minimal when the relaxant was infused via a central venous catheter (patients 9 and 10). It is important to prime all connecting tubing with relaxant and best to infuse into a running drip, because a slightly higher initial oscillation sometimes seen following the first cut-in of the pump, may be due to the deadspace of the venous cannula.

Surgical diathermy did not cause problems. The Relaxograph appears quite resistant to interference but will print out in broken lines if high-frequency disturbance is detected. We were not able to detect any episodes of inappropriate control of the syringe pump induced by bursts of diathermy.

Electrical safety is an important consideration, particularly in feedback systems. The choice of a simple reed relay, rather than more complex solid-state equipment, means that there is no direct electrical continuity between the (safety tested) Relaxograph and syringe pump. An additional safety feature is that the syringe pump runs on its own rechargeable batteries.

In conclusion, a system for feedback control of neuromuscular blockade is described. It has been evaluated using atracurium and proved simple to use, safe and effective in all patients studied. Apart from the cost of the Relaxograph and syringe pump, the system can be assembled for less than £5.

Acknowledgments

The authors wish to thank the Wellcome Foundation (Scientific Services Division) for the loan of the Relaxograph and syringe pump. We are grateful to our surgical colleagues whose patients we studied, to Dr J.R. Lehane for the computer program and to the Department of Medical Illustration at the John Radcliffe Hospital.

References

1. HUGHES R, PAYNE JP. Clinical assessment of atracurium using the single twitch and tetanic responses of the adductor pollicis muscles. *British Journal of Anaesthesia* 1983; **55:** 47S–52S.
2. ALI HH, SAVARESE JJ, BASTA SJ, SUNDER N, GIONFRIDDO M. Evaluation of cumulative properties of three new non-depolarising neuromuscular blocking drugs BW A444U, atracurium and vecuronium. *British Journal of Anaesthesia* 1983; **55:** 107S–11S.
3. ASBURY AJ, LINKENS DA. Clinical automatic control of neuromuscular blockade. *Anaesthesia* 1986; **41:** 316–20.
4. DE VRIES JW, ROS HH, BOOIJ LHDJ. Infusion of vecuronium controlled by a closed-loop system. *British Journal of Anaesthesia* 1986; **58:** 1100–3.
5. CLUTTON-BROCK TH, BLACK AMS, HUTTON P. Simple feed-back control of neuromuscular block. *Proceedings of the Anaesthetic Research Society. British Journal of Anaesthesia* 1987; **59:** 135P–6P.
6. CARTER JA, ARNOLD R, YATE PM, FLYNN PJ. Assessment of the Datex Relaxograph during anaesthesia and atracurium-induced neuromuscular blockade. *British Journal of Anaesthesia* 1986; **58:** 1447–52.
7. SAVARESE JJ, GARGARIAN M, SCOTT RPF, EMBREE PB, ALI HH, BASTA SJ, SUNDER N, WEAKLY JN, BATSON AG. Efficacy of atracurium as a continuous infusion. *British Journal of Anaesthesia* 1986; **58:** 55S.

Anaesthesia, 1987, Volume 42, pages 1218–1222

Forum

Alfentanil infusions. Comparison of bolus administration of fentanyl with three alfentanil infusion regimens

M.E. Stuart-Taylor,* BSc, FFARCS, J.W. Sleigh,† FFARCS, Registrars, Shackleton Department of Anaesthetics, Southampton General Hospital, Tremona Road, Southampton.

Summary

Three different dosage regimens of alfentanil were compared with boluses of fentanyl in 80 patients who underwent a variety of surgical procedures. Alfentanil given by infusion at a rate of 7.5 µg/kg/minute for 10 minutes followed by 0.75 µg/kg/minute, was shown to provide a stable anaesthetic which minimises the use of a volatile agent for surgery that lasts more than 45 minutes.

Key words

Anaesthesia; intravenous.
Analgesics, narcotic; fentanyl, alfentanil.

Alfentanil, a potent analgesic, is cleared from the body in times comparable to those for inhalational agents and therefore offers the possibility of considerable reduction in the use of the latter, even for short procedures.[1] Its elimination half-life ($t_{1/2}\beta$) is approximately 90 minutes, which renders it very suitable for use by continuous infusion as an adjuvant to general anaesthesia. Not only may stable plasma levels be achieved rapidly but rapid recovery may be expected once the infusion is discontinued.[2]

Alfentanil and fentanyl are chemically related although they differ pharmacokinetically and pharmacodynamically. It was decided to design a trial to establish whether an infusion of alfentanil has any advantage over bolus administration of fentanyl, and what infusion rate of alfentanil gives optimum results.

Methods

Eighty patients between the ages of 17 and 65 years, weight between 45 and 99 kg and ASA grade 1 or 2, were randomly allocated to receive either fentanyl (group 1) or alfentanil (group 2). The latter group was subdivided into three sets, 2a, 2b and 2c, to receive different infusion rates of the drug. A double-blind protocol was followed.

Table 1. Distribution of patients within each group according to degree of surgical stimulation.

	Degree of surgical stimulation*			
Group	1 (least)	2	3	4 (most)
1	3	4	4	9
2a	1	4	6	9
2b	3	5	4	8
2c	0	6	3	11

No significant difference between groups in the distribution of operations with different degrees of surgical stress using the Chi-squared test with Yates' correction. * 1 (least), repair of fractured zygoma, carpal tunnel decompression, insertion of receiver for spinal stimulation, arthroscopy, repair of finger tendon, correction of squint; 2, internal fixation fracture, removal of wisdom teeth, ligation of varicose veins, laparoscopy, mastectomy, thyroidectomy; 3, removal of cervical rib, orchidopexy, herniorrhaphy, laminectomy, vaginal prolapse repair, apronectomy, axillary clearance; 4 (most), laparotomy, cholecystectomy, hemicolectomy, abdominal hysterectomy.

The types of operations performed varied and are presented in Table 1, classified into four groups according to the degree of surgical stimulation.

Each patient was premedicated with lorazepam 1–2.5 mg orally 90 minutes pre-operatively. A 16-gauge cannula was inserted into a vein in the non-dominant

---

* Present address: Department of Anaesthetics, Basingstoke Hospital, Basingstoke, Hants RG24 9NA.

† Present address: Department of Anaesthetics, Godfrey Huggins School of Medicine, University of Zimbabwe, Harare, Zimbabwe.

0003–2409/87/111218 + 08 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

arm. Bolus injection and infusion solutions of opioid or placebo were prepared by an independent operator so that, for each patient, there was a 50-ml syringe that contained either saline (group 1) or alfentanil (groups 2a, b, c), a 10-ml syringe of fentanyl (group 1) or saline (groups 2a, b, c) marked 'X' for induction, plus a 10-ml syringe of fentanyl (group 1) or alfentanil (groups 2a, b, c) marked 'Y' for bolus top-ups during the maintenance phase of anaesthesia. The infusion solutions were made up in the following way: group 1, 50 ml saline; group 2a, 25 ml alfentanil (12.5 mg) + 25 ml saline; group 2b, 37.5 ml alfentanil (18.5 mg) + 12.5 ml saline; group 2c, 50 ml alfentanil (25 mg).

An infusion of Hartmann's solution and the 50-ml syringe of alfentanil or placebo were connected via a catheter and a three-way tap. The syringe was driven by an Injectomat syringe pump (Dylade Medical, Runcorn, Cheshire).

Anaesthesia was induced in all groups by rapid administration of 1% methohexitone to an endpoint of abolition of the eyelash reflex (range 60–120 mg). Each patient's trachea was intubated after suxamethonium 1 mg/kg. Muscle relaxation was maintained with vecuronium 5–8 mg initially, then subsequent boluses of 1–2 mg. The lungs were artificially ventilated and anaesthesia was maintained with nitrous oxide 66% in oxygen.

At induction each patient was given 0.06 ml/kg of solution from syringe 'X' as a bolus injection. This contained either fentanyl 50 μg/ml (group 1) or saline (groups 2a, 2b, 2c). Simultaneously the syringe infusion was started at a rate of 1.2 ml/kg/hour for 10 minutes. This contained either saline (group 1) or alfentanil in the concentrations outlined above (groups 2a, 2b, 2c). Therefore, each patient received an opioid either as a bolus injection of fentanyl or as a rapid induction infusion of alfentanil.

After 10 minutes the syringe infusion rate was decreased to 0.12 ml/kg/hour, i.e. 10% of its original rate, and this was continued until approximately 20 minutes before the end of surgery. Additional analgesia was provided by boluses from syringe 'Y'; therefore, group 1 received increments of fentanyl and groups 2a, b and c received increments of alfentanil. This is summarised in Table 2. The decision to administer extra opioid was made on the presence of the following signs: increase in pulse rate above 100 beats/minute; elevation of mean arterial blood pressure by more than 10% of the pre-induction value; sweating, lacrimation or pupillary dilatation; any body movement. If the additional opioid did not appear to reverse these signs, halothane 0.5–1% or enflurane 0.5–2% was added until either the above indications disappeared or surgery was completed.

Arterial blood pressure and pulse rate were recorded prior to induction and every 3 minutes throughout anaesthesia. The ECG and end tidal carbon dioxide concentration were displayed continuously and ventilation adjusted to maintain normocapnia. The slow infusion of alfentanil or placebo was discontinued approximately 20 minutes before the end of surgery and residual muscle relaxation was reversed by neostigmine 2.5 mg and atropine 1.2 mg.

Atropine 0.2–0.6 mg was given peroperatively if significant bradycardia was detected, namely, if arterial pressure was adversely affected or the pulse rate decreased below 50 beats/minute. Additional increments of neostigmine 1.25–2.5 mg were administered, without atropine, after reversal of the anaesthetic if residual muscle paralysis was thought to be present as indicated by weak hand grip or weakness of head-raising. A nerve stimulator was used if there was any doubt about the degree of reversal of muscle paralysis. Naloxone 0.4 mg was given in the presence of miosis and adequate reversal of neuromuscular blockade if apnoea or a respiratory rate less than 10 breaths/minute was seen more than 5 minutes after reversal of the anaesthetic.

Duration of surgery was taken from the first skin incision to insertion of the last suture. Duration of anaesthesia was taken from the start of the infusion to the administration of neostigmine and atropine.

Speed of recovery from the anaesthetic was assessed by measurement of the following times after reversal of muscle relaxation: time to open eyes to command, to take first spontaneous breath, to move left thumb to command, to give correct date of birth and to give correct day of week.

In the recovery area the patients were given oxygen 3 litres/minute via a Hudson mask until fully awake. Papaveretum 10–20 mg intramuscularly 3–4-hourly and perphenazine 2.5 mg were given as requested by each patient. Times of the first administration of either of these drugs were noted. Analgesic requirements were monitored in the postoperative period and patients classified into those who did not require analgesia,

Table 2. Dosage regimens of fentanyl, alfentanil and saline in the four groups.

Group	Induction	Maintenance
1	Fentanyl 3 μg/kg + fast placebo infusion of saline	Boluses of fentanyl (50–100 μg) as required + slow placebo infusion of saline
2a	Infusion 5 μg/kg alfentanil for 10 minutes + placebo bolus of saline	Infusion 0.5 μg/kg/minute alfentanil + boluses of alfentanil (500–1000 μg) as required
2b	Infusion 7.5 μg/kg alfentanil for 10 minutes + placebo bolus of saline	Infusion 0.75 μg/kg/minute alfentanil + boluses of alfentanil (500–1000 μg) as required
2c	Infusion 10 μg/kg alfentanil for 10 minutes + placebo bolus of saline	Infusion 1 μg/kg/minute alfentanil + boluses of alfentanil (500–1000 μg) as required

those who needed analgesia within the first hour postoperatively and those who needed analgesia more than one hour after surgery. Postoperative antiemetic requirements were analysed similarly. Each patient was indirectly questioned during the postoperative visit to establish whether there was any recall of events or awareness during anaesthesia.

Statistical analysis. Continuously variable data, such as demographic details and time intervals, were analysed using Student's *t*-test. Recovery indices were transformed logarithmically and then analysed using one-way analysis of variance (ANOVA). Frequencies were compared using the Chi-squared test and Fisher's exact test with Yates' correction as appropriate.

Results

The demographic data for patients in each group are shown in Table 3. Mean values for duration of surgery, duration of infusion, overall duration of general anaesthesia and the time interval between the end of the infusion and reversal of the anaesthetic, are shown in Table 4. There are no significant differences between the groups in the set of data shown in these Tables. There was no statistical difference in the distribution of the four types of surgery between the groups.

Table 5 shows that the number of patients who required incremental top-ups was less in groups 2b and 2c, although only in the latter was this statistically significant. The only group which did not require the use of a volatile agent was group 2b.

All groups had similar requirements for atropine. The types of dysrhythmia seen in this study included 2:1 block, wandering pacemaker, and asystole that lasted about 10 seconds. This latter incident resolved spontaneously. However, atropine 0.6 mg was given over the next few minutes in order to increase the heart rate which was in sinus rhythm at 43 beats/minute. There were other occasions when bradycardia or dysrhythmia was noted but they were of such short duration that treatment was not deemed necessary. Their incidence was greatest in group 1 ($n = 9$) compared with four patients in each of groups 2a and 2b, and five in group 2c. This did not reach statistical difference.

The use of naloxone was greatest in groups 1 (fentanyl) and 2c (highest concentration of alfentanil) (Table 5). Two patients in group 2a demonstrated the problem of delayed respiratory depression: they appeared to recover rapidly from the general anaesthetic but stopped breathing some time after they were transferred to the recovery area. In each case this was treated successfully with naloxone and no subsequent opioid antagonist was required.

Recovery times, shown in Table 6, did not differ significantly between the groups. There were no instances of recall or awareness. There was no statistically significant difference between groups as concerns requirements for postoperative analgesia or antiemetic therapy (Table 7).

Discussion

The infusion rates of alfentanil used in this study were determined from pharmacokinetic and pharmacodynamic data which show that a plasma level of alfentanil of approximately 300 ng/ml is needed to maintain adequate surgical anaesthesia for patients whose lungs are ventilated with nitrous oxide 60% in oxygen.[3] We aimed, therefore, for a range of infusion rates that encompassed this value using two consecutive constant-rate infusions. Our protocol was modified from that used in a multicentre trial organised by the manufacturers.

The results in Table 5 show that the fentanyl group contained the largest number of patients who required opioid supplements as well as the use of a volatile agent. When the three infusion regimens for alfentanil are compared, group 2b had the least number of

Table 3. Demographic data. Values expressed as mean (SEM).

	Group 1 ($n = 20$)	Group 2a ($n = 20$)	Group 2b ($n = 20$)	Group 2c ($n = 20$)
Age, years	40.6 (2.87)	45.1 (2.46)	42.2 (2.92)	34.6 (2.38)
Weight, kg	67.9 (2.3)	68.1 (1.97)	62.7 (1.97)	67.6 (2.71)
Sex, M:F	7:13	9:11	4:16	5:15

No significant differences between drug groups using Student's *t*-test.

Table 4. Durations of general anaesthesia, surgery and infusions, and time interval between cessation of infusion and reversal of anaesthesia. Values expressed as mean (SEM).

	Group 1	Group 2a	Group 2b	Group 2c
Duration of anaesthesia, minutes	92.6 (13.61)	74.9 (4.94)	85.8 (8.45)	85.4 (13.5)
Duration of surgery, minutes	73.0 (11.95)	56.5 (4.5)	59.5 (7.5)	65.6 (11.4)
Duration of infusion, minutes	58.4 (12.0)	41.65 (4.25)	48.3 (7.22)	50.5 (11.46)
End of infusion–reversal interval, minutes	24.7 (2.92)	23.3 (1.88)	24.4 (2.15)	24.9 (2.9)

No significant differences between drug groups using Student's *t*-test.

patients who needed supplementary anaesthetic whether it be additional opioid or a volatile agent. This is confirmed by other studies. For example, Ausems and Hug[4] used infusion rates of alfentanil that correspond to group 2b in this study and found that only one out of 15 patients required supplementary volatile agent at the time of opening the abdominal wall. Furthermore, despite the short distribution half-life ($t_{1/2}\alpha$) of alfentanil of approximately 12 minutes,[3] there was no statistically significant increase in the need for, or timing of, postoperative analgesia (Table 7).

The episode of asystole for a period of 10 seconds mentioned earlier, occurred in a fit, 35-year-old man undergoing a laminectomy. This is a serious side effect of the drug but the dysrhythmia was too brief to affect the arterial pressure significantly and sinus rhythm resumed spontaneously. In addition to the few patients who needed atropine, others experienced bradydysrhythmia which did not warrant treatment. An increasing number of drugs now used by anaesthetists have been observed to be associated with bradydysrhythmias. In one case report asystole occurred when vecuronium was used in the absence of any phenylpiperidine drug.[5] In view of this, we recommend the use of an anticholinergic agent in the premedication for cases known to be associated with vagal stimulation, such as ophthalmic surgery, but otherwise to be prepared to administer a vagolytic agent if necessary.

Most patients in all groups displayed a reduction in arterial pressure of less than 15% of the pre-induction value between induction and surgical incision. In no case was a vasopressor needed. This stability was confirmed by de Lange and de Bruijn.[6] In our study there were four cases when the arterial pressure decreased by 45% from the pre-induction value. They involved one patient on beta-blockade therapy (group 1), one with poorly controlled hypertension (group 2a) and two who were dehydrated patients over the age of 60 years (group 2b). In each of these the arterial pressure recovered with surgical stimulation.

The results from our informal methods of assessment of recovery showed no significant difference between the groups. This is confirmed by the results of other studies that have used more formal techniques.[7,8]

There have been several reports on respiratory depression following alfentanil.[9,10] In the present study, groups 1 and 2c required naloxone significantly more often than did the other two groups. This was seen either in patients who required multiple bolus top-ups or in whom the infusion was stopped 9 minutes before reversal of the anaesthetic. Two patients (both older than 60 years) received the lowest alfentanil infusion rates and became apnoeic in the recovery area within 15 minutes of reversal of the anaesthetic. They responded to naloxone 0.2 mg intravenously and the same dose intramuscularly and showed no further signs of respiratory depression. Unlike the case for fentanyl, there does not appear to be a delayed secondary peak in plasma alfentanil concentrations associated with respiratory depression and, as confirmed in a study by Valgardsson *et al.*,[11] the patient is unlikely to suffer from a recurrence of respiratory depression as a result of the alfentanil alone if he has recovered well after the first hour. Thus, diligent postoperative care is still needed in these patients and we recommend that this infusion technique is not used in patients over the age of 60 years.

We conclude that an opioid infusion is superior to bolus administration in that it produces smooth

Table 5. Incidence of patients who required volatile agents or supplementary opioid, atropine or naloxone.

	Group 1	Group 2a	Group 2b	Group 2c
Number of bolus top-ups	16	16	9	6*
Volatile agent	6	4	0*	4
Atropine	3	2	2	1†
Naloxone	6	2*	1*	4

* $p < 0.05$ using Fisher's exact test. † Asystole that lasted for 10 seconds.

Table 7. Comparison of numbers of patients who required antiemetic or analgesic therapy within the first hour and after one hour postoperatively.

	Group 1	Group 2a	Group 2b	Group 2c
Antiemetic				
0–60 minutes	7	5	5	9
> 60 minutes	4	7	8	2
None	9	8	7	9
Analgesic				
0–60 minutes	12	10	6	13
> 60 minutes	5	9	9	2
None	3	1	5	5

No statistical difference between groups using the Chi-squared test with Yates' correction.

Table 6. Comparison of average speed of recovery (minutes) in the four groups (see text for explanation). Values expressed as mean (SEM).

	Group 1	Group 2a	Group 2b	Group 2c
Opening eyes	5.40 (1.12)	3.25 (0.66)	3.05 (0.70)	4.35 (0.69)
First spontaneous breath	4.90 (1.09)	3.18 (0.58)	3.15 (0.72)	3.65 (0.68)
Thumb movement	7.20 (1.26)	6.90 (2.32)	7.65 (2.63)	5.26 (0.70)
Date of birth	10.3 (2.01)	11.4 (4.24)	11.8 (2.66)	6.84 (1.08)
Day of week	11.6 (2.34)	9.55 (2.47)	13.9 (3.18)	8.16 (1.20)

No significant difference between groups using logarithmic transformation and ANOVA.

anaesthesia with more stable cardiovascular parameters, reduced requirements for volatile agents and more predictable recovery. Furthermore, the infusion rates of alfentanil used in group 2b of this study offer the best compromise between quality of anaesthesia and quality of recovery.

Acknowledgments

The authors thank Dr D. A. Saunders, Southampton General Hospital, and Dr C. Chapfield, University of Bath, for their help with statistical analysis, and also Dr S. Linter for assistance with the idea. The help of Janssen Pharmaceuticals Ltd is acknowledged for supplies of alfentanil and for their permission to extend this study from their multicentre trial.

References

1. Sanders RS, Sinclair ME, Sear JW. Alfentanil in short procedures. A comparison with halothane using etomidate or methohexitone for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1202–6.
2. Hug CC Jr. Pharmacokinetics and pharmacodynamics of narcotic analgesics. In: Prys-Roberts C, Hug CC Jr, eds. *Pharmacokinetics of anaesthesia*. Oxford: Blackwell Scientific Publications, 1984: 187–234.
3. Bovill JG, Sebel PS, Blackburn CL, Heykants J. The pharmacokinetics of alfentanil (R39209): a new opioid analgesic. *Anesthesiology* 1982; **57**: 439–43.
4. Ausems ME, Hug CC. Plasma concentrations of alfentanil required to supplement nitrous oxide anaesthesia for lower abdominal surgery. *British Journal of Anaesthesia* 1983; **55**: 191S–7S.
5. Clayton D. Asystole associated with vecuronium. *British Journal of Anaesthesia* 1986; **58**: 937–8.
6. De Lange S, de Bruijn NP. Alfentanil–oxygen anaesthesia: plasma concentrations and clinical effects during variable-rate continuous infusion for coronary artery surgery. *British Journal of Anaesthesia* 1983; **55**: 183S–9S.
7. Kay B, Venkataraman P. Recovery after fentanyl and alfentanil in anaesthesia for minor surgery. *British Journal of Anaesthesia* 1983; **55**: 169S–71S.
8. Antonios WRA, Inglis MD, Lees NW. Alfentanil in minor gynaecological surgery: use with etomidate and a comparison with halothane. *Anaesthesia* 1984; **39**: 812–4.
9. Sebel PS, Lalor JM, Flynn PJ, Simpson BA. Respiratory depression after alfentanil infusion. *British Medical Journal* 1984; **289**: 1581–2.
10. Raeder JC, Hole A. Alfentanil anaesthesia in gallbladder surgery. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 35–40.
11. Valgardsson A, Werner O, Svensson G. Antagonism of fentanyl and alfentanil by intravenous plus subcutaneous naloxone. Pattern of ventilatory depression after a short procedure. *Anaesthesia* 1985; **40**: 772–6.

Anaesthesia, 1987, Volume 42, pages 1222–1225

Anaesthetic management for carbon dioxide laser surgery in tracheobronchial lesions

J. Hunton, MB, BS, FFARCS, Consultant Anaesthetist, South Cleveland Hospital, Marton Road, Middlesbrough, Cleveland, V.H. Oswal, FRCS, DLO, Consultant ENT Surgeon, North Riding Infirmary, Newport Road, Middlesbrough, Cleveland.

Summary

There are technical difficulties associated with anaesthesia in patients who undergo laser surgery to the trachea and main bronchi using the carbon dioxide laser. An anaesthetic technique using spontaneous ventilation is described which has been used successfully in 33 patients.

Key words

Surgery; trachea, laser.

The carbon dioxide laser is used increasingly in endoscopic surgery. Modifications to the anaesthetic technique are necessary when the laser coupler is attached to a bronchoscope. This report describes our experience in carbon dioxide laser bronchoscopy in procedures undertaken for obstructive lesions of the trachea and main bronchi.

The Coherent 450 laser endoscopic coupler contains a series of high precision mirrors which reflect and focus the laser beam to a 2-mm spot at 300 mm distance. When the coupler is attached to a Wolf bronchoscope, a large leak is introduced into the anaesthetic system which makes intermittent positive pressure ventilation (IPPV) via the ventilation port of the bronchoscope impossible. It is necessary, therefore, to block off the coupler in order to isolate it from the anaesthetic system. This is achieved by introducing a gas shield, which fits into a slot provided in the coupler (Fig. 1). The material needed to form the gas shield must transmit the laser light and yet withstand its heat.

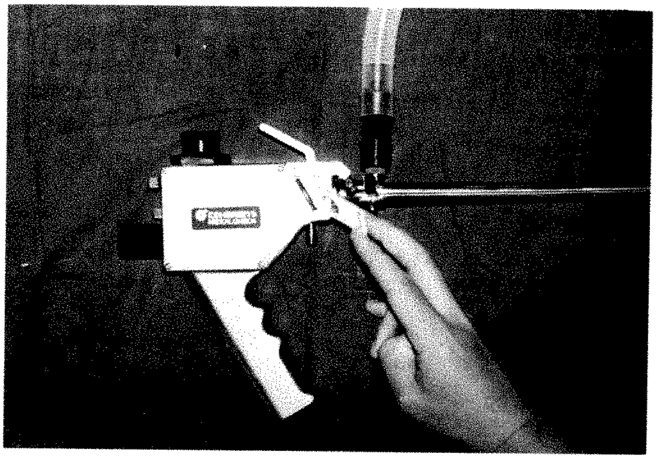


Fig. 1. The laser coupler attached to a Wolf bronchoscope and coaxial anaesthetic system (Penlon), with a gas shield placed into its slot.

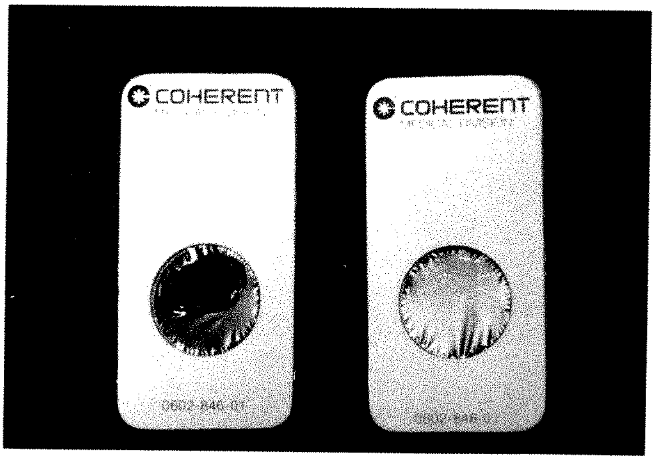


Fig. 2. Magnified view of the gas shield before use (*right*) and after a short period of laser use.

t is made of mylar membrane (Dupont) held in a ardboard surround. This material has laser trans- ıissive characteristics but perforates within seconds f continuous laser usage (Fig. 2). The life of the ıembrane may be extended if it is vibrated using a jet f air generated by an independent air pump.

The integrity of the anaesthetic system is lost and ıe gas shield must be replaced as soon as the mem- rane perforates. The integrity of the system is also ›st when the surgeon detaches the coupler to remove :cretions, blood or debris, to refocus the laser or to ssess progress. The total time taken for a broncho- :opic resection may be as long as 90 minutes. Removal f the coupler may take place many times during the rocedure and, with the additional leaks through the ıs shield, it is extremely difficult to maintain IPPV adequately. We have devised a method of anaesthesia for such procedures in which spontaneous ventilation is maintained.

Patients and methods

The majority of our patients had advanced pulmonary malignancy complicated by airway obstruction. The aim of treatment was purely palliative and for relief of symptoms (mainly dyspnoea); consequently, no patient was assessed as unfit for general anaesthesia on medical grounds. Initially, patients were lightly premedicated with a tranquilliser/antisialogogue combination because of concern that an opioid might precipitate respiratory failure. However, there were some instances of awareness and, as experience was gained, standard opioid/antisialogogue premedication was used in the majority of patients without any untoward effects.

Anaesthesia

Anaesthesia was induced with thiopentone, and tracheal intubation with a cuffed red rubber tracheal tube facilitated with suxamethonium. The tracheal tube was removed immediately before introduction of the Wolf bronchoscope and the coaxial tube of a Bain anaesthetic system was connected to the side arm of the bronchoscope. IPPV was continued until the return of spontaneous breathing. At this stage all proximal openings of the bronchoscope must be blocked off. A Forregger cuff has been used around the distal end of the bronchoscope. However, we found that when an air-tight seal around the bronchoscope is required, wet gauze swabs, placed in the pharynx, adequately prevent leaks in the absence of a Forregger cuff. General anaesthesia was maintained with the patient breathing spontaneously a mixture of nitrous oxide, oxygen and halothane at a fresh gas flow of 20 litres/minute. The expiratory valve on the coaxial system was closed, which introduces a degree of continuous positive airway pressure (CPAP). Monitoring of electrocardiogram (ECG) and automatic indirect blood pressure measurement were standard. Blood gas analysis was undertaken on four patients.

In one patient, gas samples from the distal end of the bronchoscope were taken during and between laser use. The samples were analysed using gas chromatography in order to detect breakdown products of the anaesthetic gases.

Results

To date, 33 patients have been anaesthetised by this method for laser surgery. There was no anaesthetic mortality, although there was one peri-operative death due to uncontrollable haemorrhage in a patient with a thyroid carcinoma that invaded the trachea.

Gas chromatography (Fig. 3) revealed that breakdown products of halothane were produced. Halogenated ethane and ethylene molecules were detected in concentrations of between 1 and 2% of the halothane concentration. The compound in highest concentration in Fig. 3 is CF_3CH_2Cl. The largest peak is that of halothane.

Blood gas analysis showed that the arterial carbon dioxide tension ($P\text{aco}_2$) increased from pre-anaesthetic levels but remained within acceptable limits. The peak $P\text{aco}_2$ ranged from 6.5 to 8.9 kPa. With a maximum inspired oxygen concentration of 40%, arterial oxygen tension was between 17 and 20 kPa.

Discussion

Intermittent positive pressure ventilation is regarded by many anaesthetists as the preferred technique for patients who undergo prolonged endoscopic surgery. Some of the procedures in the present study lasted for more than 90 minutes and few were shorter than 20 minutes. It is technically difficult to use IPPV with the Wolf bronchoscope and Coherent laser coupler because of the mechanics of the coupler. Standard insufflators that use the Venturi system cannot be used with this bronchoscope because of the coupler. However, it is possible to modify the insufflator for inser-

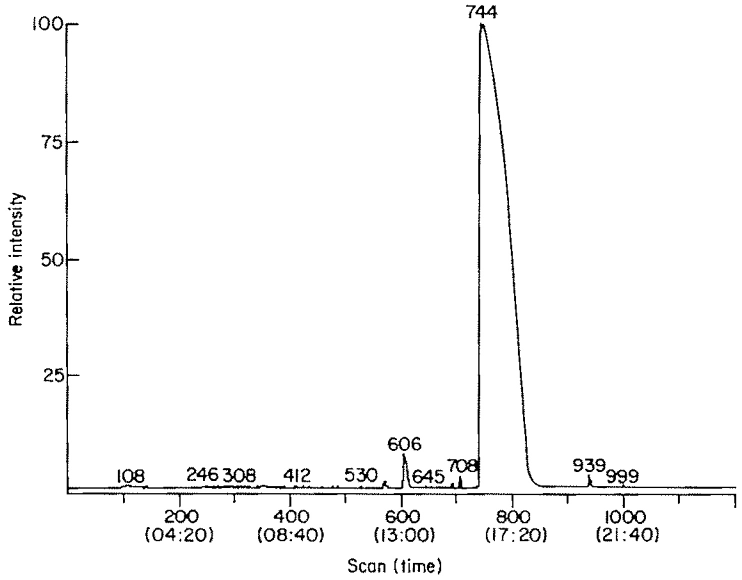


Fig. 3. Gas chromatograph showing several peaks, the largest of which is halothane. The second largest peak is a halogenated ethane molecule.

tion into the lumen of the bronchoscope via the side ventilation port. The presence of the Venturi within the bronchoscope is likely to increase the difficulty of focussing the laser, add to problems of reflection and interfere generally with the surgical view and access. A ventilator for the Wolf bronchoscope has been described[1] and is marketed by Litechnica Ltd. The proximal end of the bronchoscope is modified to abut the laser coupler. Ventilation requires a further modification by the addition of a 2-mm conduit that extends the length of the outer wall to within 1 cm from the tip. This pipe acts as a ventilation system, smoke extractor and suction channel. High frequency positive pressure ventilation has been used successfully for laser bronchoscopy.[2] However, this is appropriate only for neodymium–YAG laser surgery, where the fibreoptic bronchoscope is passed through the rigid scope. Other workers have used the same lumen-sharing technique.[3–5]

Anaesthesia using spontaneous ventilation has many theoretical disadvantages. Patients with severe airways obstruction or low compliance would be expected to respond poorly with increased work of breathing and poor gas exchange. The interaction between either nitrous oxide or the volatile agent and the laser may be disadvantageous, as indeed may be an increased inspired oxygen concentration. Vourc'h *et al.*[4] advocated the replacement of nitrous oxide with nitrogen. Since the carbon dioxide laser generates heat it is theoretically possible to generate free radicals from its interaction with halothane. In the present study, gas chromatography detected the presence of halogenated ethane and ethylene compounds. We noted no toxic effects, although this aspect is the subject of further study since it is likely that a range of compounds may be produced. Theoretically, oxides of nitrogen may also be produced by lasers in the presence of nitrous oxide.

Initially, we considered blood gas analysis to be essential. However, the first few analyses demonstrated that the technique maintained acceptable blood gases and we ceased routine testing.

A major advantage of this technique is that the high fresh gas flow rate removes smoke continuously from the surgical field at such a rate as to afford an excellent view, and thereby reduces surgical time. On occasion, it has been possible to place the bronchoscope beyond the tumour, which decreases obstruction to ventilation; the resection has then proceeded in a retrograde manner.

There were a number of episodes of inadequate ventilation, hypotension, dysrhythmias and circulatory collapse prior to the introduction of the present technique. With the introduction of spontaneous breathing, such events are no longer encountered, possibly because the method produces more reliable gas exchange than did attempts at IPPV via the ventilation port.

Acknowledgment

The authors are grateful to ICI, Wilton for conducting the gas chromatography studies.

References

1. Paes ML, Conacher ID, Snellgrove TR. A ventilator for carbon dioxide laser bronchoscopy. *British Journal of Anaesthesia* 1986; **58:** 663–9.
2. Vourc'h G, Fischler M, Michon F, Melchior JC, Seigneur F. Manual jet ventilation v. high frequency jet ventilation during laser resection of tracheo-bronchial stenosis. *British Journal of Anaesthesia* 1983; **55:** 973–5.
3. Sia RL, Edens T, Van Overbeek JJM, Rashkovsky OM. Three years' experience with the Groningen Nd YAG laser coagulation technique. *Anaesthesia* 1985; **40:** 904–6.
4. Vourc'h G, Tannieres ML, Toty L, Personne C. Anaesthetic management of tracheal surgery using the neodymium–yttrium–aluminium–garnet laser. *British Journal of Anaesthesia* 1980; **52:** 993–7.
5. Dumon JF, Reboud E, Garbe L, Aucomte F, Meric B. Treatment of tracheobronchial lesions by laser photoresection. *Chest* 1982; **81:** 278–84.

Anaesthesia, 1987, Volume 42, pages 1226–1243

Correspondence

Cardiovascular collapse following epidural anaesthesia for Caesarean section 1226
D. Brighouse, FFARCS
C.R. Grebenik, FFARCS, C. Orlikowski, FFARCS and J.D. Barber, FFARCS 1227
M.D. Mitchell, FFARCS and J.W. Downing, FFARCS 1228
M.N.E. Harris, FFARCS 1229
J.W. MacKenzie, MRCP 1229
J.S. Crawford, FFARCS, FRCOG 1229
J.D. Alderson, FFARSI 1230
Nitrous oxide and hearing loss 1230
A.J. Coe, FFARCS
Identification of the epidural space 1231
C.M. Wait, FFARCS
Fixed dilated pupils following cardiac surgery 1231
C.A. Carter, FFARCS and G.A. Weston, FFARCS
Consent for epidural analgesia 1232
J.R. Sneyd, FFARCS
Propofol in failed tracheal intubation 1233
P. Coleman, FFARCS and B. Phillips, FFARCS
Absence of clinically significant neonatal respiratory depression after prolonged maternal propofol administration 1233
G.K. Bloor, MB, BS, M.J. Jones and D.A.B. Turner, FFARCS
Oxygenation during electroconvulsive therapy 1234
K.H. Simpson, FFARCS, S.N. Chater, FFARCS and S.R. Swindells, FFARCS
C.D. Hanning, FFARCS, J. Lew, FFARCS and R.J. Eastley, FFARCS 1234
Depression, anxiety and chronic pain 1235
T.M. Jack, FFARCS, V.A. Walker, BSc, SRN, SCM, S.J. Morley, PhD, G.W. Hanks, MRCP and B.M. Finlay-Mills, BSc
Pancuronium and renal failure 1236
W. Sangala, FFARCS and J. Dixon, FFARCS
J.M. Hunter, FFARCS 1236
The effect of benzodiazepines on evoked potentials 1237
K.R. Milligan, FFARCS, R.C. Howard, PhD and J.W. Dundee, PhD, FRCP, FFARCS
P.S. Sebel, PhD, FFARCSI 1237
Capnography 1238
C.M.S. Cooper, BSc, MB, BS
Serological markers for hepatitis B 1239
G.N. Newcombe, MB, BS, DRCOG
An unusual cause of upper airways obstruction 1239
L.M. Aldridge, FFARCS, DCH
An improved antipollution device for the Jackson–Rees modification of the Ayre's T-piece 1240
P.M. Spargo, FFARCS, A. Apadoo and H.J. Wilton, FFARCS
Isoflurane in a drawover anaesthesia system 1241
S. Yoganathan, FFARCS, RAMC and I.T. Houghton, FFARCS, RAMC
Complications of difficult intubation 1241
S.M. Mostafa, FFARCS
AIDS and anaesthesia 1242
J.J. Luke, FFARCS and J.M. Cundy, FFARCS
Postmortem removal of tracheal tube 1242
K.R. Johnston, FFARCS
P. Charters, FFARCS 1242
Difficult tracheal intubation 1243
W.F.S. Sellers, FFARCSI and S. Yogendran

Cardiovascular collapse following epidural anaesthesia for Caesarean section

One has considerable sympathy with Dr Alderson (*Anaesthesia* 1987; **42:** 643–5) and I appreciate that wisdom with hindsight is easy; nevertheless, the management of the case he describes requires some comment.

The patient had severe pre-eclampsia (proteinuria

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

greater than 3 g/24 hours, plus diastolic blood pressure 90 mmHg or more).[1] Pre-eclamptic patients are known to have deranged fluid balance and may have coagulopathy, which would contraindicate epidural anaesthesia. No mention is made of clotting status in this patient.

It might have been prudent to institute direct blood pressure monitoring via an arterial cannula prior to insertion of the epidural catheter in view of the risk of hypotension inherent in any regional technique and the potentially disastrous consequences of such hypotension. Interpretation of central venous pressure readings may be difficult but insertion of a right atrial catheter is desirable in severely pre-eclamptic patients, and the gross discrepancy between the atrial pressures on the two sides of the heart in severe aortic incompetence may be an indication for pulmonary artery catheterisation.

Injection of a single bolus dose of 18 ml 0.5% bupivacaine might be considered incautious in this case. An incremental technique as described by Moir[2] is less likely to be complicated by hypotension and may have avoided the problem of inadequate sacral block. An alternative method of managing inadequate sacral block which I have found useful on occasion, would have been caudal injection of the second increment of bupivacaine.

The supine wedged position cannot be recommended in the face of the severe hypotension which occurred in this patient; further hypotension due to aortocaval compression can be avoided only by adoption of the full lateral position.

Dr Alderson is to be complimented on maintaining a cardiac output in his patient by cardiac massage for so long. Recent work has highlighted the problems of effective cardiac massage on patients in the lateral position.[3] Any attempt to maintain cardiac output by massage whilst the patient is supine is, of course, fruitless before delivery, since aortocaval compression occurs. Finally, Dr Alderson should be thanked for being brave enough to publish details of a maternal death. Full consideration of the circumstances that surround such an event can only help avert further tragedies.

John Radcliffe Hospital,
Oxford OX3 9DU

D. Brighouse

References

1. Davey DA, Dommisse J, Opie L. Severe hypertension, pre-eclampsia and eclampsia. In: Baldwin RWM, Hanson GC, eds. *The critically ill obstetric patient*. London: Farrand Press, 1984: 248.
2. Moir DD. *Obstetric anaesthesia and analgesia*, 2nd edn. London: Baillière Tindall, 1980: 216.
3. Rees GAD. Cardiopulmonary resuscitation. *Symposium on safer obstetric anaesthesia*. Faculty of Anaesthetists of the Royal College of Surgeons of England, 1986.

We were interested to read Dr Alderson's case report (*Anaesthesia* 1987; **42:** 643–5) but disagree with his conclusion that epidural anaesthesia is contraindicated in patients with symptomatic aortic incompetence.

In the case described the patient presented with hypertension and a murmur of aortic incompetence. Her pregnancy was further complicated by the development of pre-eclampsia and heart failure, and she was also noted to have mitral incompetence and left ventricular hypertrophy.

In our opinion fluid loading prior to establishment of an epidural block was contraindicated in this patient who was on the verge of heart failure and had not been given her morning diuretics. Administration of a large volume of crystalloid solution was inappropriate and might have precipitated pulmonary oedema.

The initial dose of bupivacaine (18 ml of 0.5% plus 2 ml test dose) was excessive. Dr Alderson states correctly that a reduction in systemic vascular resistance is beneficial in aortic insufficiency since the amount of regurgitant flow is decreased. However, this applies only to a mild and gradual reduction in vascular resistance since a sudden and profound decrease will cause a marked reduction in arterial pressure, as happened in this case. Hypotension and a low diastolic pressure reduce coronary perfusion pressure and may cause myocardial ischaemia. This patient's left ventricle was dilated and hypertrophied since it was compromised by both pressure and volume overload, and was therefore particularly susceptible to decreases in coronary blood flow. Subendocardial ischaemic changes were confirmed at postmortem. In addition, the rapid decrease in arterial pressure would have compromised placental blood flow and put the mother at risk of stroke.

The first bolus dose of bupivacaine produced sensory blockade to T_4; autonomic blockade would extend cephalad to the sensory block for several segments,[1] so that cardiac sympathetic denervation would have occurred. This is detrimental for two reasons. Firstly, this patient was reliant on sympathetic drive to support her failing heart, as shown by her documented intolerance to labetalol (which has predominantly β-blocking effects with only mild α blockade[2]). Secondly, the decrease in sympathetic tone could have caused bradycardia. Patients with aortic incompetence tolerate bradycardia poorly since the increase in the length of diastole allows a greater proportion of the cardiac output to become regurgitant. Hence effective cardiac output decreases greatly. There is no record of this patient's heart rate after initiation of the block.

The appropriate treatment for the decrease in blood pressure and cardiac output would have been the early administration of an α-adrenergic agonist to restore coronary perfusion pressure and, if required, a β agonist to increase heart rate and myocardial contractility. Monitoring of pulmonary capillary wedge pressure would have guided pharmacological support and fluid loading.

The final dose of bupivacaine was given with the patient supported sitting up to encourage caudal spread. The effects of gravity on spread of local anaesthetic solutions within the epidural space are minimal[3] and this further dose produced total cardiovascular collapse. It is not surprising that resuscitation was unsuccessful.

In our opinion a carefully managed epidural block undertaken with appropriate monitoring, attention to volume status, incremental small doses of local anaesthetic and the use of vasopressors to avoid a sudden and severe decrease in arterial pressure would have resulted in a successful conclusion. A full understanding of the pathophysiology involved in an extremely complex case such as this is vital for safe management of either epidural or general anaesthesia.

St. Bartholomew's Hospital, C.R. Grebenik
West Smithfield, C. Orlikowski
London EC1A 7BE J.D. Barber

References

1. Chamberlain DP, Chamberlain BDL. Changes in the skin temperature of the trunk and their relationship to sympathetic blockade during spinal anesthesia. *Anesthesiology* 1986; **65**: 139–43.
2. Goodman and Gilman. *Pharmacological basis of therapeutics*, 7th edn. New York: Macmillan, 1985.
3. Norris MC, Dewan DM. Effect of gravity on the spread of extradural anaesthesia for caesarean section. *British Journal of Anaesthesia* 1987; **59**: 338–41.

Dr Alderson's case report (*Anaesthesia* 1987; **42**: 643–5) highlights many of the problems in the management of the complicated cardiac parturient. However, we consider that his suggestion that epidural anaesthesia is contraindicated in the presence of aortic incompetence, even with concomitant pre-eclampsia, represents a disservice to obstetric anaesthesia for the following reasons.

Experience gained in the care of the poorly compensated cardiac parturient and patients with severe pre-eclampsia at King Edward VIII Hospital, Durban, where such problems are encountered commonly, leads us to believe that carefully managed epidural blockade is the technique of choice for parturients not only with aortic incompetence but also with almost all types of severe cardiac pathology and pregnancy related hypertension. This view is supported by the experience of other workers in this field.[1–4]

Epidural anaesthesia should be instituted slowly and deliberately as advocated by others,[5,6] with small increments of local anaesthetic given at well spaced intervals. Injection of a large bolus of local anaesthetic will frequently cause significant hypotension even in fit mothers[6] and can prove lethal if cardiac function is impaired.[7] Bolus injection may produce toxic levels of bupivacaine, due either to systemic absorption or to accidental intravenous injection.[8]

The minimum monitoring standard for the obstetric cardiac patient should mandate central venous pressure measurement.[9] Symptomatic patients (New York Heart Association grades III and IV[10]) require further invasive haemodynamic monitoring[1–3,11] in the form of right atrial, direct arterial and pulmonary artery wedge pressure measurements, as well as thermodilution cardiac output determinations. Pulmonary artery oximetry, if available, would be considered desirable. Cannulation of both arteries and central veins can be performed rapidly and easily under local anaesthesia without undue distress to the patient.[12] Baseline haemodynamic measurements taken before epidural blockade act as guidelines to the correct degree of intravenous preloading required by each individual patient.

Hypovolaemia must be avoided if at all possible; treatment of hypotension must be prompt and aggressive should blood pressure decrease. Patient posture in the left lateral tilt position with the legs raised, intravenous fluid infusion and finally vasoconstrictor therapy guided by right atrial and pulmonary artery wedge pressures, will usually restore the blood pressure to acceptable levels.

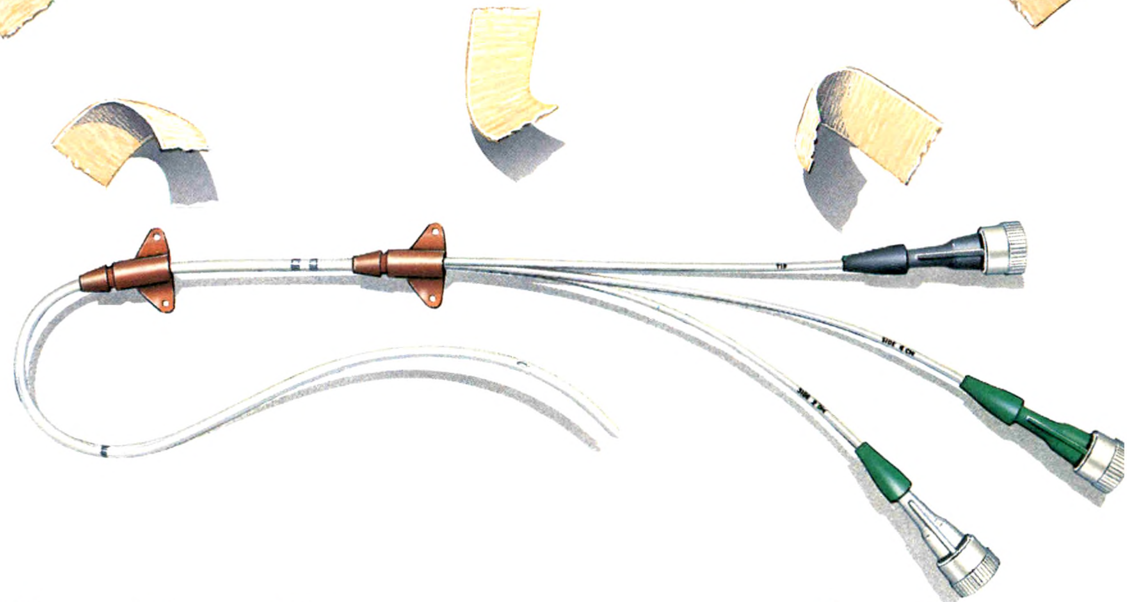
In conclusion, we wish to stress the importance of appropriate haemodynamic monitoring, control of cardiac filling pressures and a small incremental epidural dose schedule whenever extradural anaesthesia is used in obstetrics, for both healthy and sick pregnant patients. Any approach which transgresses these basic premises for patient safety constitutes, in our view, a recipe for disaster which could unnecessarily tarnish the reputation of epidural anaesthesia, which has proved to be a highly satisfactory and safe technique in experienced hands.

Queen's Medical Centre, M.D. Mitchell
Nottingham NG7 2UH J.W. Downing

References

1. Hanson GC. Systems for monitoring the critically ill mother. In: Baldwin RWM, Hanson GC, eds. *The critically ill obstetric patient*. London: Farrand Press, 1984: 73–95.
2. Joyce TH III. Cardiac disease. In: James FM III, Wheeler AS, eds. *Obstetric anesthesia: the complicated patient*. Philadelphia: F.A. Davis Co., 1982: 87–101.
3. Mangano DT. Anesthesia for the pregnant cardiac patient. In: Shnider SM, Levinson G, eds. *Anesthesia for obstetrics*, 2nd edn. Baltimore: Williams and Wilkins, 1987: 343–81.
4. James FM III. Pregnancy induced hypertension. In: James FM III, Wheeler AS, eds. *Obstetric anesthesia: the complicated patient*. Philadelphia: F.A. Davis Co., 1982: 249–67.

Hydrocath®



Only the name sticks.

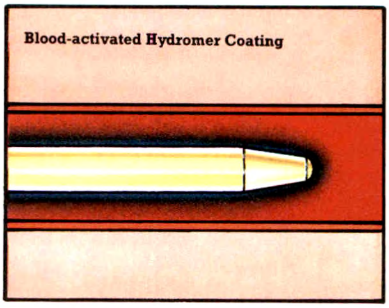
HYDROMER® is the special hydrophilic polymer that protects all HYDROCATH® catheters. When activated by body fluids it creates an aqueous complex which surrounds the catheter.

This complex reduces the surface friction of the catheter to less than that of wet glass, making insertion easier and reducing patient trauma.

Once in situ the Hydromer coat remains activated, creating a barrier at the blood/catheter interface.

For more information on the complete range of Secalon® Hydrocath central venous catheters please telephone (0793) 641791 or write to "Hydrocath", Viggo, P.O. Box 77, Swindon, Wiltshire, U.K.

® = Registered Trademark

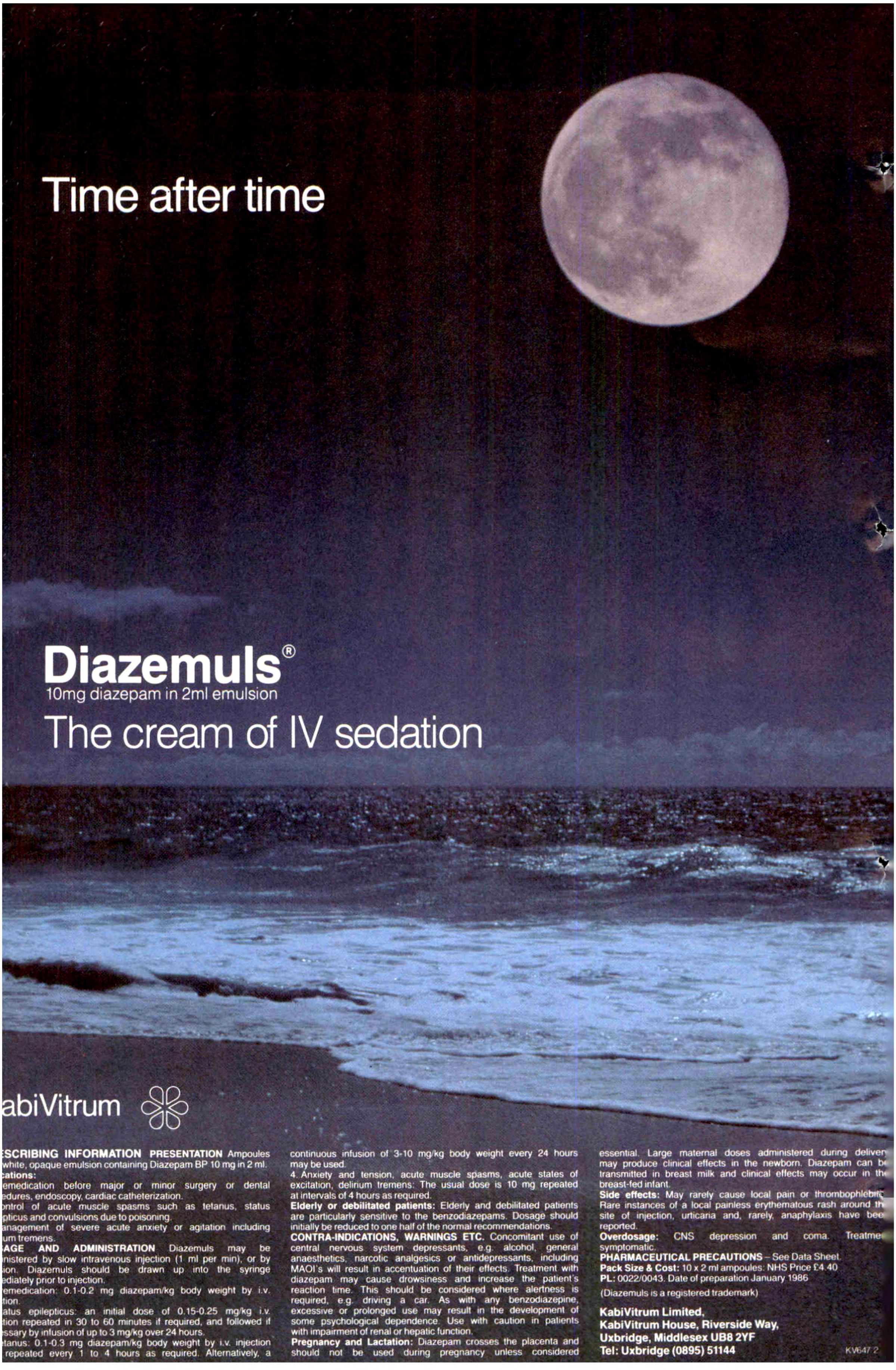


Viggo

British Viggo
Faraday Road
Swindon
Wiltshire SN3 5HZ
Tel: 0793 641791
Telex: 444443 VIGGO G

BOC Health Care

Viggo International Sales
Chertsey Road
Windlesham
Surrey GU20 6HJ
Tel: 0276 77222
Telex: 859363 BOC GHQ G
Fax Nos: 0276 71333/77550



SCRIBING INFORMATION PRESENTATION Ampoules
white, opaque emulsion containing Diazepam BP 10 mg in 2 ml.
cations:
emedication before major or minor surgery or dental
edures, endoscopy, cardiac catheterization.
ontrol of acute muscle spasms such as tetanus, status
pticus and convulsions due to poisoning.
anagement of severe acute anxiety or agitation including
um tremens.
AGE AND ADMINISTRATION Diazemuls may be
nistered by slow intravenous injection (1 ml per min), or by
ion. Diazemuls should be drawn up into the syringe
ediately prior to injection.
emedication: 0.1-0.2 mg diazepam/kg body weight by i.v.
tion.
atus epilepticus: an initial dose of 0.15-0.25 mg/kg i.v.
tion repeated in 30 to 60 minutes if required, and followed if
ssary by infusion of up to 3 mg/kg over 24 hours.
tanus: 0.1-0.3 mg diazepam/kg body weight by i.v. injection
repeated every 1 to 4 hours as required. Alternatively, a continuous infusion of 3-10 mg/kg body weight every 24 hours may be used.

4. Anxiety and tension, acute muscle spasms, acute states of excitation, delirium tremens: The usual dose is 10 mg repeated at intervals of 4 hours as required.

Elderly or debilitated patients: Elderly and debilitated patients are particularly sensitive to the benzodiazepams. Dosage should initially be reduced to one half of the normal recommendations.

CONTRA-INDICATIONS, WARNINGS ETC. Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics or antidepressants, including MAOI's will result in accentuation of their effects. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. This should be considered where alertness is required, e.g. driving a car. As with any benzodiazepine, excessive or prolonged use may result in the development of some psychological dependence. Use with caution in patients with impairment of renal or hepatic function.

Pregnancy and Lactation: Diazepam crosses the placenta and should not be used during pregnancy unless considered essential. Large maternal doses administered during deliver
may produce clinical effects in the newborn. Diazepam can b
transmitted in breast milk and clinical effects may occur in th
breast-fed infant.

Side effects: May rarely cause local pain or thrombophlebit
Rare instances of a local painless erythematous rash around th
site of injection, urticaria and, rarely, anaphylaxis have bee
reported.

Overdosage: CNS depression and coma. Treatme
symptomatic.

PHARMACEUTICAL PRECAUTIONS – See Data Sheet.
Pack Size & Cost: 10 x 2 ml ampoules: NHS Price £4.40
PL: 0022/0043. Date of preparation January 1986

(Diazemuls is a registered trademark)

KabiVitrum Limited,
KabiVitrum House, Riverside Way,
Uxbridge, Middlesex UB8 2YF
Tel: Uxbridge (0895) 51144

KV647 2

5. Thorburn J, Moir DD. Epidural analgesia for elective Caesarean section. Technique and assessment. *Anaesthesia* 1980; **35:** 3–6.
6. Albright GA. Lumbar epidural anesthesia. In: Albright GA, Ferguson JE, Joyce TH, Stevenson DK, eds. *Anesthesia in obstetrics: maternal, fetal and neonatal aspects*, 2nd edn. Boston: Butterworths, 1986: 278–309.
7. Alderson JD. Cardiovascular collapse following epidural anaesthesia for Caesarean section in a patient with aortic incompetence. *Anaesthesia* 1987; **42:** 643–5.
8. Lavies NG. Speed of epidural injection. *Anaesthesia* 1987; **42:** 783–4.
9. De Swiet M. Cardiorespiratory disease. In: Morgan B, ed. *Perinatal practice, Vol. 3. Problems in obstetric anaesthesia*. Chichester: John Wiley and Sons, 1986: 139–47.
10. New York Heart Association, Criteria Committee. *Diseases of the heart and blood vessels: nomenclature and criteria for diagnosis*, 6th edn. Boston: Little Brown, 1964: 112–3.
11. Ferguson JE II, Wyner J, Albright GA, Brodsky JB. Maternal health complications. In: Albright GA, Ferguson JE, Joyce TH, Stevenson DK, eds. *Anesthesia in obstetrics: maternal, fetal and neonatal aspects*, 2nd edn. Boston: Butterworths, 1986: 374–420.
12. Wallace PG. Anaesthesia for cardiac surgery. In: Smith G, Aitkenhead AR, eds. *Textbook of anaesthesia*. Edinburgh: Churchill Livingstone, 1986: 386.

The recent case report of an intra-operative death by Dr Alderson (*Anaesthesia* 1987; **42:** 643–5) concluded that epidural anaesthesia may be contraindicated for Caesarean section in patients with symptomatic aortic incompetence.

Surely it is not the epidural that is contraindicated, but an anaesthetic technique that fails to provide adequate monitoring and hence appropriate cardiovascular intervention in the face of both severe cardiac disease and an operation that causes major alterations of pressure, resistance and work to the left and right sides of the heart? Monitoring of arterial, central venous and pulmonary capillary wedge pressures is essential if this sort of disaster is to be avoided, combined with an ability to intervene appropriately and immediately with drugs and fluids on the basis of the information derived from such monitoring.

It is obvious that these patients represent a very high risk and I would suggest that they should always be managed in an intensive care unit by an experienced anaesthetist; the type of anaesthesia administered is secondary to this.

St. Thomas' Hospital, M.N.E. Harris
London SE1 7EH

Dr Alderson is aware that hypotension due to reduction in total peripheral resistance is undesirable, but that this did occur in this case seems likely since the block reached T_4 within 15 minutes following a bolus of 18 ml 0.5% plain bupivacaine.

Sympathetic blockade usually extends two segments rostrally beyond the analgesic level[1] and the block may not even have reached its full extent at 15 minutes. Subdural block may have occurred[2] and the second dose further compromised the patient. A block of the upper thoracic sympathetic outflow prevents the reflex vasoconstriction in vessels subserved from these segments which in less extensive epidural blocks serves to minimise changes in total peripheral resistance,[3] and thereby maintain blood pressure.

We are told that the patient weighed 55 kg and so presumably was below average height. Regional anaesthesia may well be indicated in such a patient with cardiac failure but adequate monitoring (as employed in this case) and careful administration of anaesthetic agents to minimise predictable adverse effects are necessary whatever anaesthetic technique is adopted.

The likelihood of inadvertent development of high epidural block may be minimised by employing a through-catheter incremental dosing technique which, although it entails establishing the block more slowly, must surely be safer in such at risk cases.

Royal Berkshire Hospital, J.W. MacKenzie
Reading,
Berks RG1 5AN

References

1. Churchill-Davidson HH, ed. *A practice of anaesthesia*. Lloyd Luke Ltd, 1985.
2. Lee A, Dodd KW. Accidental subdural catheterisation. *Anaesthesia* 1986; **41:** 847–9.
3. Shimasato S, Etsten BE. The role of the venous system in cardiocirculatory dynamics during spinal and epidural anesthesia in man. *Anesthesiology* 1969; **30:** 619–28.

For years now, Dr D. Moir, myself and many others have emphasised the overwhelming importance of injecting a local anaesthetic into the epidural space in incremental doses. Even had the patient reported by Dr Alderson not had a severe cardiac lesion there was a good chance that she would have been rendered hypotensive by the bolus injection of 18 ml 0.5% bupivacaine. She had a rapidly extending vasomotor block, as evidenced by its reaching to the upper thoracic level within 15 minutes and, of significant importance, had received only one litre of Hartmann's solution as a preload. That was tantamount to giving her a spinal and exemplifies why I will not advocate spinals for Caesarean section.

The lesson to be learned from this case is not, as Dr Alderson avers, that an epidural is contraindicated in the circumstances described, but that the block must be induced in small increments, which allows time for stabilisation of cardiovascular dynamics after each top-up. Such intervals, in our experience, are 15–20 minutes. Haste, apart from being unnecessary, leads to disaster.

Had our persistent advocacy been heeded the patient would have, in my opinion, been less likely to have come to harm.

Birmingham Maternity Hospital,
Birmingham B15 2TG
J.S. CRAWFORD

A reply

Thank you for giving me the opportunity to reply. The intention of the case report was to provoke discussion on the use of epidural anaesthesia in patients with aortic incompetence so I was pleased to find that it had generated comments.

Monitoring of the cardiovascular system intra-operatively is criticised as being inadequate in that it lacked central venous pressure (CVP) and (or) pulmonary capillary wedge pressure monitoring. The patient had been in hospital for some time and repeated blood sampling (daily) had greatly reduced the usability of veins on both arms. The use of internal jugular or subclavian vein was considered but would have been difficult technically in view of her short neck and the dyspnoea from heart failure which prevented her from lying completely flat. It was felt that insertion of such a line might well cause more problems than it prevented; these lines are not without complications of their own, to say nothing of the anxiety the attempt at insertion might provoke (her heart rate before, during and after insertion of the epidural was 110 beats/minute, as reported). It is, however, my normal practice to use CVP monitoring, via antecubital fossa if possible, for both severe pre-eclampsia and severe cardiac disease. Intra-arterial monitoring was not thought to offer any advantage over satisfactory non-invasive automatic oscillotonometry.

Many anaesthetists prefer to institute epidural anaesthesia for Caesarean section by an incremental dose technique. These techniques theoretically allow time for stabilisation of cardiovascular dynamics after each top-up but, to my knowledge, their final cumulative effect on the systemic vascular resistance does not differ from that produced by single epidural injections of larger volumes. Some centres may follow the incremental injection technique but there are also others who use single large bolus injection as practised in this case, and others who would use spinal anaesthesia. If my theory as to the cause of cardiovascular collapse in aortic incompetence is correct, as supported by the findings of the Spanish cardiac surgery team,[1] that reduction of systemic vascular resistance causes a marked reduction in coronary blood flow leading to myocardial ischaemia, then this would surely occur no matter which method of regional anaesthesia was employed. It was for this reason that the case was reported. The use of an α-adrenergic agonist such as phenylephrine may well be the treatment of choice in such an unfortunate situation.

Northern General Hospital,
Sheffield S5 7AU
J.D. ALDERSON

Reference

1. RUFILANCHAS JJ, VILLAGRA F, MARONAS JM, TELLEZ G, AGOSTI J, JUFF A, FIGUERA D. Coarctation of the aorta and severe aortic insufficiency: what to repair first? *American Journal of Surgery* 1977; **134**: 428–30.

Nitrous oxide and hearing loss

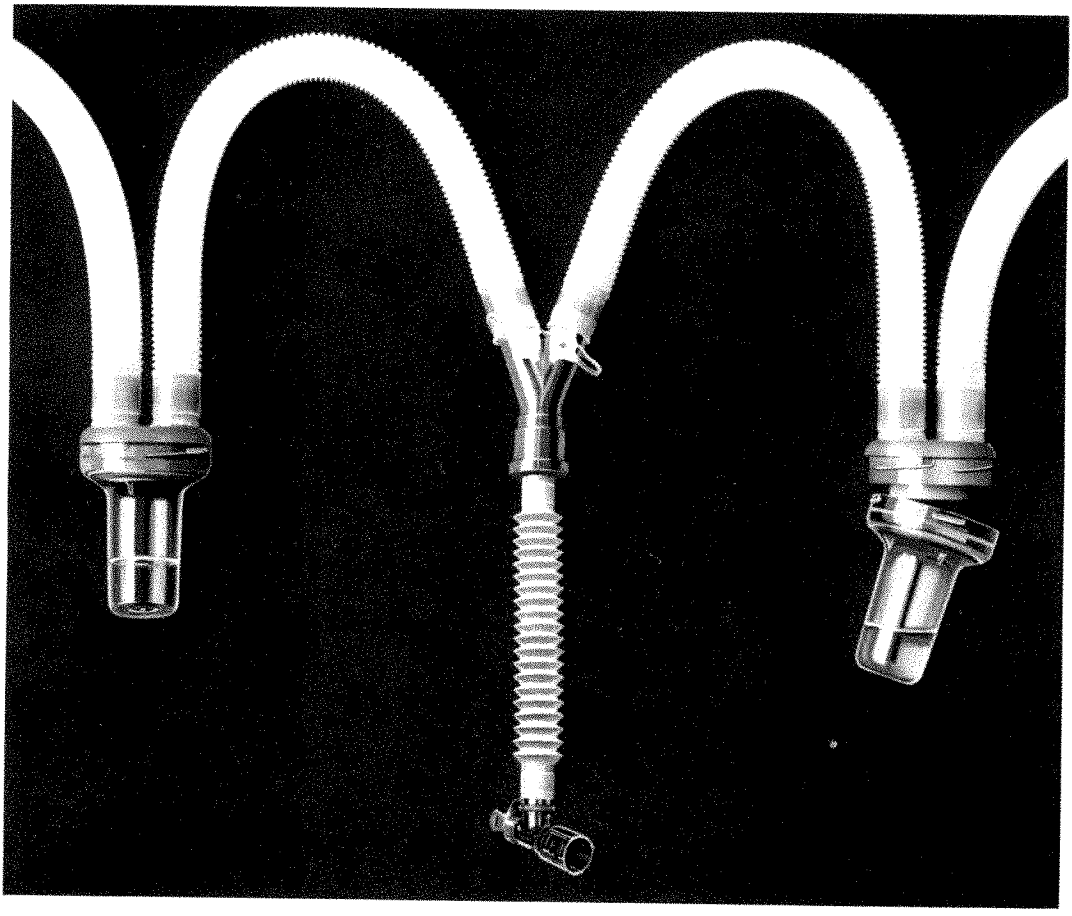
Permanent conductive hearing loss has been reported after nitrous oxide anaesthesia in patients who have stapes prostheses in their middle ear cavities.[1,2] Nitrous oxide anaesthesia is known to increase middle ear pressure,[1] and may thus cause movement or dislocation of the prosthesis.

The case notes of 57 patients with stapes prostheses *in situ* were examined for audiometric evidence of conductive hearing loss after subsequent nitrous oxide anaesthesia to assess the extent of this problem. Eight patients had missing or incomplete audiometric records. Twelve of the remaining 49 patients were given nitrous oxide anaesthetics in the years following their stapes surgery. Ten of these 12 had no evidence of hearing loss after nitrous oxide exposure. However, three of these 10 patients had lost so much hearing anyway that further loss would be undetectable. They had 90 decibel or more reductions in sensitivity to air-conducted sound. Four of this group of 10 patients underwent examinations of the middle ear cavity under anaesthesia, which included a tympanotomy. Increases in middle ear pressure would be unlikely in this situation.

This left five patients who were genuinely at risk of hearing loss, two of whom showed clearly measurable deterioration. One patient showed a decrease in sensitivity to air-conducted sound of 20–30 decibels on audiograms taken 5 months before and 9 months after an abdominal hysterectomy. Inspection of the middle ear cavity immediately after the second audiogram showed a dislocated prosthesis.

This does not prove that nitrous oxide caused the changes but the coincidence is hardly reassuring for those who would ignore the problem. On the other hand, this small retrospective study highlights the fact that not all patients are at risk, either because they have lost most of their hearing anyway or because the procedure involves a tympanotomy. It also shows that

DO YOU NEED A RELIABLE BREATHING SYSTEM READY FOR USE DAY OR NIGHT?



Then we have the answer . . .

Disposable ventilator and anaesthetic systems pre-assembled ready for immediate use.

- *Eliminate the fear of cross infection*
- *Cut out costly time-consuming sterilisation*
- *Circuits may be custom built to suit your own specific requirements*
- *All connector fittings are safe and secure, manufactured to meet BS3849 specifications*
- Ⓐ *And GMP registration gives you the assurance of high quality*

Reliability combined with cost-effectiveness, it must make sense

REMEMBER IN HEALTH CARE – QUALITY COUNTS.

Intersurgical

COMPLETE RESPIRATORY SYSTEMS

Crane House Gould Road Twickenham Middlesex
England TW2 6RS Tel 01-755 1477
Telex 8953147 INTERS G

RING FOR SAMPLE 01-755 1477

Pain management in hospital and the home

Spembly Medical is foremost in the discipline of Pain Management. The Company has earned a unique reputation for its development of high quality instrumentation, particularly for the techniques of Cryoanalgesia and TENS.

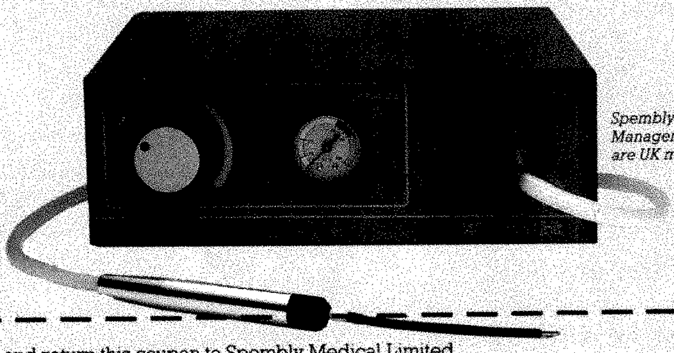
An excellent example is the SL2000 Lloyd Neurostat. It adds a new perspective to the management of both acute and chronic pain via localised freezing of nerves. Treatment by Cryoanalgesia is of particular benefit for relieving post-operative pain and in conditions such as facet rhizolysis, coccydynia and neuroma formation.

Equally, the Spembly Medical 140 Cryounit, used in conjunction with the Maiwand probe, is an established method of freezing the intercostal nerves prior to closing the thorax — a recognised means of providing post-thoracotomy pain relief.

Obtaining pain relief, without recourse to drugs, through treatment by TENS is rapidly increasing. Outstanding for this technique is the Pulsar range — a family of small, lightweight battery operated units which enable more patients to obtain greater benefits from TENS over a wider range of clinical conditions. Significantly, Spembly Medical is the first to have designed a special unit for use in Obstetrics.

Spembly medical

Spembly Medical Limited
Newbury Road, Andover, Hampshire,
SP10 4DR, England
Telephone: (0264) 66741 Telex: 47403



Spembly Medical Pain Management products are UK manufactured.

Please clip and return this coupon to Spembly Medical Limited,
Newbury Road, Andover, Hampshire, SP10 4DR, England, for more details on:— GP/A/11

☐ SL2000 Lloyd Neurostat ☐ 140 Cryounit ☐ TENS Pulsar ☐ Obstetric Pulsar

NAME POSITION

ADDRESS

TELEPHONE

not all at risk patients will suffer hearing loss. The trouble and expense of anaesthesia without nitrous oxide is certainly justified in these patients, after those with very poor conductive hearing and those listed for tympanotomy on the relevant side have been excluded.

Southmead Hospital,
Bristol

A.J. Coe

References

1. Davis I, Moore JRM, Lahiri SK. Nitrous oxide and the middle ear. *Anaesthesia* 1979; **34:** 147–51.
2. Patterson ME, Bartlett PC. Hearing impairment caused by intratympanic pressure changes during general anesthesia. *Laryngoscope* 1976; **86:** 399–404.

Identification of the epidural space

This is a simple refinement of the loss of resistance technique for identification of the epidural space.

Most anaesthetists employ some variation of the technique described by Sicard and Forestier[1] and then popularised by Dogliotti.[2] It is customary to test for the loss of resistance to injection with a syringe that contains either saline or air. However, some disadvantages attend the use of either medium.

Saline is incompressible so it is possible to confuse a glass syringe plunger that is jammed with one that is incompressible because the tip of the needle is in tough ligamentum flavum. This situation may lead to accidental dural puncture.[3] The use of saline can also result in an occasional artefactual loss of resistance, particularly if the midline approach is used. The mechanisms that underly such 'pseudo-loss of resistance' remain fully to be elucidated.[4–6]

The use of an air-filled glass syringe immediately identifies a sticky plunger and also permits the detection of more subtle variations in resistance within the tissues. However, the injection of air into the epidural space may result in a patchy block if bubbles prevent local anaesthetic solution making contact with one or more nerve roots.[7] Saline is said to distend the epidural space and facilitate the passage of a catheter.[3] The same may not apply to air. Other reported complications of the use of air include venous air embolism[8] and surgical emphysema.[9]

These various considerations have led me to modify my own technique to test routinely for loss of resistance with a saline-filled glass syringe (Everett 10 ml, Avon Medicals Ltd, Redditch, England) into which a small bubble of air has been introduced. This simple expedient confers a degree of compressibility on the syringe contents which restores the 'bounce' to the plunger and improves the sensitivity of the technique. It is *saline* that is injected when the epidural space is located, because the air bubble floats in the syringe above the level of the needle hub. Thus the virtues of both air and saline are retained while their disadvantages are discarded.

Radcliffe Infirmary,
Oxford OX2 6HE

C.M. Wait

References

1. Sicard JA, Forestier J. Méthode radiographique d'exploration de la cavité épidurale par le lipiodol. (Radiographic method for exploration of the epidural space using Lipiodol.) *Revue Neurologique* 1921; **28:** 1264–6.
2. Dogliotti AM. New method of block anesthesia; segmental peridural spinal anesthesia. *American Journal of Surgery* 1933; **20:** 107–18.
3. Bromage PR. *Epidural analgesia.* Philadelphia: W.B. Saunders Co., 1978.
4. Moore DC. *Regional block*, 4th edn. Springfield, Illinois: Charles C. Thomas, 1965: 417.
5. Davidson JT. Identification of the epidural space. *Anesthesiology* 1966; **27:** 859.
6. Sharrock NE. Recordings of, and an anatomical explanation for, false positive loss of resistance during lumbar extradural analgesia. *British Journal of Anaesthesia* 1979; **51:** 253–8.
7. *Sir Robert Macintosh's lumbar puncture and spinal analgesia*, 5th edn. Edinburgh: Churchill Livingstone, 1985: 215.
8. Naulty JS, Ostheimer GW, Datta S, Knapp R, Weiss JB. Incidence of venous air embolism during epidural catheter insertion. *Anesthesiology* 1982; **57:** 410–2.
9. Laman EN, McLeskey CH. Supraclavicular subcutaneous emphysema following lumbar epidural anesthesia. *Anesthesiology* 1978; **48:** 219–21.

Fixed dilated pupils following cardiac surgery

A 6-year-old girl who weighed 25 kg, underwent surgery for correction of an atrial septal defect and fashioning of a pulmonary arterial gusset. Anaesthesia and cardiopulmonary bypass proceeded uneventfully, except that large doses of phenylephrine (67 mg) were required to maintain an adequate perfusion pressure during the 54 minutes of bypass. The heart was thoroughly de-aired in the usual manner before withdrawal of the bypass. The child was noted to have fixed and dilated pupils at the end of the operation. The blood pressure, heart rate and arterial blood gases were satisfactory, as they had been throughout the procedure. No abnormality of pupil size or response was seen at any stage prior to induction.

She was given dexamethasone 4 mg intravenously and transferred to the intensive care unit in view of our concern that the pupil abnormality was due to an intracerebral catastrophe. Spontaneous movements of all four limbs were seen over the next 30 minutes and she opened her eyes to command. The trachea was extubated 6 hours after the end of surgery and she made a full recovery with no neurological deficit. The pupils remained dilated until 4 hours after surgery before they returned to normal size.

Atropine 0.2 mg was given intravenously at induction but this dose would be very unlikely to produce fixed and dilated pupils 3 hours later. No other drugs, such as ganglion blockers, were given that would have produced such an effect.

Phenylephrine is a direct acting α-adrenergic agonist that is used as a vasopressor during cardiopulmonary bypass. Topical phenylephrine produces dilatation of the pupil for ophthalmoscopy and the treatment of glaucoma. We believe that the large dose of phenylephrine administered during bypass in this case resulted in sufficient amounts reaching the eye from the systemic circulation to cause mydriasis.

Northern General Hospital,
Sheffield S5 7AU

C.A. Carter
G.A. Weston

Consent for epidural analgesia

Questionnaires were sent to nursing sisters in delivery suites at 100 randomly chosen hospitals which offer training in midwifery. The questions were designed to determine the usage of consent forms, the time at which such a form is signed and the identity of the person who gives any explanation to the mother. Eighty-six out of 100 hospitals replied but no follow-up to improve this figure was used. The results are summarised in Fig. 1.

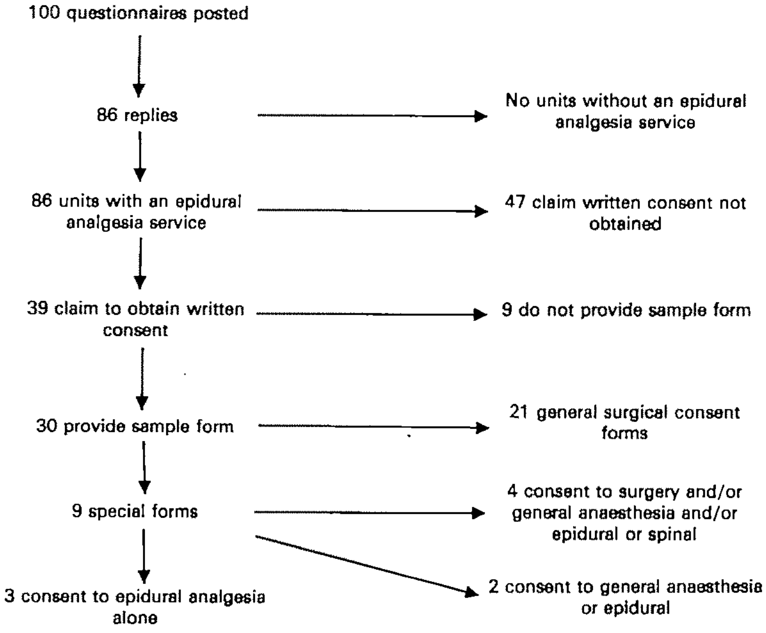

100 questionnaires posted
86 replies
No units without an epidural analgesia service
86 units with an epidural analgesia service
47 claim written consent not obtained
39 claim to obtain written consent
9 do not provide sample form
30 provide sample form
21 general surgical consent forms
9 special forms
4 consent to surgery and/or general anaesthesia and/or epidural or spinal
3 consent to epidural analgesia alone
2 consent to general anaesthesia or epidural

Fig. 1. Summary of survey results.

Written consent was obtained immediately before the epidural in 36 units. In three units, consent was obtained on admission to the delivery suite. All units claimed that the procedure was explained by doctors and midwives. Written comments suggested that some doctors gave only minimal explanation before consent was obtained.

This survey demonstrates a variety of procedures for recording consent. This diversity is in sharp contrast to general surgical practice where patients give written consent in standard wording.

Informed consent is a prerequisite for obstetric epidural analgesia. When should consent be obtained? Anybody who has ever attempted to discuss the advantages, disadvantages, side effects and possible complications of an epidural with a woman who is rolling about the bed in agony from her labour will be aware of the practical problems. Even if it were possible to obtain informed consent well in advance, further discussion would be necessary at the time of the procedure to ensure no change of heart; conversely, many women start labour resolutely opposed to epidurals but ask for one subsequently. The problem of consent

Churchill Livingstone

Latest titles to keep you up to date

The book you can't do without . . .

HAZARDS AND COMPLICATIONS OF ANAESTHESIA

Edited by T. H. Taylor and Edward Major

1987 563 pages illus
hardback £65.00

A comprehensive guide to the complications of anaethesia, highlighting the hazards and pitfalls that may be encountered.

Written by forty well known, experienced practitioners, all of whom present their topics in a form useful and relevant to the trainee and to the senior anaesthetist confronted with an unfamiliar problem.

ANAESTHESIA REVIEW 4

Edited by Leon Kaufman

1987 244 pages illus
paperback £14.95

The latest in the series of review volumes which cover the newest developments across the entire range of anaesthesia.

MANUAL OF ANAESTHESIA IN CANCER CARE

William S. Howland, Sharon Marie Rooney and Paul L. Goldiner

1987 340 pages illus
paperback £22.00

Superbly illustrated–in full colour . . .

PRINCIPLES AND PRACTICE OF REGIONAL ANAESTHESIA

Edited by J. A. W. Wildsmith and Edward N. Armitage

1987 216 pages illus (most in colour) hardback £35.00

Gives an up-to-date account of the theoretical basis of regional anaesthesia and evaluates recent research. Describes the practical applications of regional anaesthesia, giving firm guidelines about techniques and management.

THE ECG IN ANAESTHESIA AND CRITICAL CARE

Edited by Daniel M. Thys and Joel Kaplan

1987 265 pages illus
paperback £19.95

MANUAL OF ANAESTHESIA FOR EMERGENCY SURGERY

Edited by Judith H. Donegan

1987 420 pages illus
paperback £22.50

THE ANESTHESIA MACHINE

Clayton Petty

1987 235 pages over 200 illus
hardback £25.00

Due for publication early '88

INTRAVENOUS ANAESTHESIA

John W. Dundee and Gordon M. Wyant

1988 Second edition 372 pages
illus hardback £50.00

An up-to-date survey of the pharmacology and clinical uses of the intravenous drugs used in modern anaesthetic practice.

New from the Clinics in Critical Care Medicine series

INFECTION CONTROL IN INTENSIVE CARE

Edited by Bruce F. Farber

1987 215 pages illus
hardback £23.50

GASTROINTESTINAL EMERGENCIES

Edited by C. W. Imrie and A. R. Moossa

1987 200 pages illus
hardback £25.00

CARDIOVASCULAR PROBLEMS IN PEDIATRIC CRITICAL CARE

Edited by David B. Swedlow and Russell C. Raphaely

1986 311 pages 80 illus
hardback £35.00

711AN/A

Medical Division of Longman Group Ltd. Registered Office: 5 Bentinck Street, London W1M 5RN.
Registered No: 872828 England.

Churchill Livingstone

New From **ACADEMIC PRESS.........**

ADVANCES IN DRUG RESEARCH

Volume 16

Edited by **Bernard Testa**
Sept 1987, 500pp., 0.12.013316.4, £45.00 (tentative)

From the Reviews of Volume 14:
"..... This is an excellent book..... It is recommended reading for all medicinal chemists." JOURNAL OF MEDICINAL CHEMISTRY

CONTENTS: Preface: The Scientist as Alexander and Weaver, **B. Testa.** Free Radicals in Drug Design, **M. Roberfroid, H.G. Viehe and J. Remacle**. The Parametrization of Lipophilicity and other Structural Properties in Drug Design, **H. Van de Waterbeemd and B. Testa**. Structure-activity Relationships and Mechanisms of Action Antibacterial Sulphanilamides and Sulphones, **P.G. Benedetti**. The Stereoelectronic Effects at the Opiate Receptor: Their Influence on Affinity and Intrinsic Activity, **V.M. Kolb**. Drug Action and Cellular Calcium Regulation, **R.A. Janis, P. Silver and D.J. Triggle**.

Volume 15

Edited by **Bernard Testa**
1986, 256pp., 0.12.013315.6, £30.00/$54.00

CONTENTS: Toxication Mechanisms in Drug Metabolism. Elements for the Rational Design of Peptide Drugs. Tissue and Receptor Selectivity: Similarity and Differences. Inhibition of Prostaglandin, Thromboxane, and Leukotriene Biosynthesis. Foodstuffs as Sources of Psychoactive Amines and Their Precursors: Content, Significance and Identification. Index.

Volume 14

Edited by **Bernard Testa**
1984, 352pp., 0.12.013314.8, £50.00/$78.00

CONTENTS: Deterium Isotope Effects in the Metabolism of Drugs and Xenobiotics: Implications for Drug Design. Drug Design in Three Dimensions. Mechanisms of Action of Antiinflammatory Drugs. Recent Advances in the Molecular Pharmacology of Benzodiazepine Receptors and in the Structure-Activity Relationships of their Agonists and Antagonists. Index.

For further information on these titles please write to:
Academic Press Ltd., One Vincent Square, London SW1P 2PN, U.K.

is demonstrated by one patient who instructed the author that she did not wish to have an epidural, no matter how much she might scream for one.

Should consent be in writing? The act of signing a form does not prove informed consent. Conversely, the lack of a signature does not necessarily mean that there was not consent. We do not ask for written consent before insertion of a central line, aspiration of a pleural effusion or ordering an intravenous urogram, yet these procedures are no less hazardous than epidural analgesia. In contrast, we invariably obtain written consent (in hospital practice) for minor surgery such as removal of small skin lesions under local anaesthetic.

If we want consent in writing then an appropriate wording should be used. There is little point in collecting signatures on forms which refer to 'the operation' and to 'further procedures that may be found to be necessary'. Disclaimers like 'no assurance has been given to me that the operation will be performed by any particular practitioner' serve only to confuse and worry the patient.

In a litigious age it is desirable that consent be recorded. The words 'informed consent obtained' with date, time and signature entered in the notes are no less meaningful than a signature on a general surgical consent form.

The present diversity of practice is undesirable. The profession should decide whether or not it wants written consent before obstetric epidural analgesia; if it does, a standard form of words should be used.

Sherrington School of Physiology,
St. Thomas' Hospital,
London SE1 7EH

J.R. Sneyd

Propofol in failed tracheal intubation

The failed intubation drill for obstetric patients in our unit is very similar to that described by Tunstall.[1] However, we were concerned that maintenance of anaesthesia with inhalational agents, if this were appropriate, might prove technically difficult particularly in the period between the recovery from suxamethonium and the establishment of surgical anaesthesia.

The new intravenous anaesthetic agent, propofol, may prove useful in these circumstances either as the sole anaesthetic agent or to smooth the transition to a volatile anaesthetic. A controlled trial would not be ethical to test this suggestion but we recently had the opportunity to evaluate the technique during an unexpected failed intubation in a patient who presented for emergency Caesarean section for fetal distress.

The patient was a fit, 44-year-old, 38-week pregnant multigravida who weighed 92 kg, with no overt anatomical abnormalities of the oropharynx and no previous anaesthetic that required tracheal intubation. The larynx could not be seen after a standard rapid sequence induction with thiopentone and suxamethonium and attempts at tracheal intubation were abandoned after 2 minutes. The lungs were gently ventilated by hand with 100% oxygen until spontaneous ventilation returned. Increments of propofol 20–30 mg were then given to a total of 200 mg while enflurane was introduced. Anaesthesia proceeded smoothly without coughing or laryngospasm. A live male infant was delivered with Apgar scores of 6 at 1 minute and 9 at 5 minutes. Operative blood loss was less than 600 ml. The mother had an uneventful recovery.

We consider, in the light of this experience, that propofol may have a place in obstetric anaesthesia.

Walton Hospital,
Rice Lane,
Liverpool L9 1AE

P. Coleman
B. Phillips

Reference

1. Tunstall ME. Failed intubation drill. *Anaesthesia* 1976; 31: 850.

Absence of clinically significant neonatal respiratory depression after prolonged maternal propofol administration

Propofol has been infused for sedation during regional anaesthesia[1] but there are no reports of its use in intensive care during the third trimester of pregnancy, immediately prior to Caesarean section.

A 39-year-old multiparous woman of 36 weeks' gestation was admitted in respiratory distress secondary to acute pulmonary oedema, and required ventilatory support. Her clinical condition improved steadily with appropriate pharmacological therapy and intermittent positive pressure ventilation of her lungs. Monitoring included the use of a pulmonary artery flotation catheter and cardiotocography.

Once stabilised, she was sedated initially with a combination of morphine and midazolam. These were replaced with a continuous infusion of propofol 2–3 mg/kg/hour for 20 hours prior to Caesarean section, in an attempt to avoid neonatal respiratory depression. The patient was sufficiently sedated to tolerate tracheal intubation but remained responsive and co-operative. In total 3 g of propofol were infused. There was no change in pulmonary artery pressure or wedge pressure.[2]

Meconium staining was noted at operation and a normal 2.67-kg female infant was delivered. Apgar scores were 7 at 1 minute and 9 at 5 minutes. Cord blood pH was 7.21.

Propofol is not licensed for long-term sedation but the potential beneficial effect to the neonate by avoidance of respiratory depression in the immediate postdelivery period induced by other sedative agents justified its use in this situation.

Leicester Royal Infirmary,
Leicester LE1 5WW
G.K. BLOOR
M.J. JONES
D.A.B. TURNER

References

1. MACKENZIE N, GRANT IS. Propofol for intravenous sedation. *Anaesthesia* 1987; **42:** 3–6.
2. STEPHAN H, SONNTAG H, SCHENK HD, KETTLER D, KHAMBATTA HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; **58:** 969–75.

Oxygenation during electroconvulsive therapy

We would like to comment on some of the points raised in recent correspondence concerning oxygenation during electroconvulsive therapy (ECT) (*Anaesthesia* 1987; **42:** 431–2). Drs Wood and Sneyd suggested that hypoxaemia during ECT may be prevented if patients' lungs were ventilated with 100% oxygen rather than 40–60%. However, Drs Hanning, Lew and Eastley postulated that the small increase in oxygen stores would be unlikely to protect all patients from hypoxaemia, particularly if the seizure was prolonged.

We observed a decrease in transcutaneous oxyhaemoglobin saturation of more than 5% from the baseline value in 16 cases in a study of 40 patients who received anaesthesia and ECT, despite ventilation with 100% oxygen using a Mapleson C system prior to the shock but not during the seizure.[1] Surprisingly, desaturation did not correlate with seizure duration, which ranged from 6–80 seconds. Hypoxaemia occurred when the number of passive ventilations given prior to administration of the shock was inadequate; most of the hypoxaemic patients received fewer than 10 passive ventilations. Therefore, hypoxaemia can occur during ECT even if 100% oxygen is administered; however, we considered that this was unlikely if care was taken to ventilate adequately prior to the shock.

Thirty patients in a recent study were pre-oxygenated until a transcutaneous oxyhaemoglobin saturation of 98% was achieved and then, on three separate occasions, they received either no further ventilation, or 10 or 20 passive ventilations of 100% oxygen from a non-rebreathing system.[2] Ventilation was resumed when the seizure stopped. Transcutaneous oxyhaemoglobin saturation remained above 90% in all cases during anaesthesia and the seizure. Therefore, if patients are pre-oxygenated, hypoxaemia is not a problem even if no further oxygen is administered until after the seizure. We therefore propose that ventilation during the seizure, as suggested by Drs Hanning, Lew and Eastley,[3] is not advisable, since it may increase the risk of regurgitation.

Pre-oxygenation to avoid the necessity for passive ventilation, may be applicable in patients where regurgitation is a particular risk, for example those with obesity or reflux oesophagitis, or where psychotropic drugs may cause gastric stasis. However, it must be remembered that some disturbed patients may be afraid of anaesthetic masks and unable to cooperate.

In conclusion, we consider that ventilation with 100% oxygen using a high flow system should be mandatory during anaesthesia for ECT, since hypoxaemia is not only potentially dangerous but may limit the duration of the seizure. Routine monitoring of transcutaneous oxyhaemoglobin saturation during ECT may be a valuable safeguard.

St. James University Hospital,
Leeds
K.H. SIMPSON
S.N. CHATER
S.R. SWINDELLS

References

1. SWINDELLS SR, SIMPSON KH. Oxygen saturation during electroconvulsive therapy. *British Journal of Psychiatry* 1987; **150:** 695–6.
2. CHATER SN, SIMPSON KH. An investigation of the effect of passive hyperventilation on seizure duration in patients having electroconvulsive therapy. *British Journal of Anaesthesia* 1987 (in press).
3. HANNING CD, LEW J, EASTLEY R. Oxygenation during electroconvulsive therapy. A comparison of two techniques. *Anaesthesia* 1986; **41:** 1092–7.

A reply

We find the advice of Drs Simpson, Chater and Swindells somewhat confusing. On the one hand they have shown that prolonged pre-oxygenation is necessary to prevent hypoxaemia during electroconvulsive therapy (ECT) while on the other, they admit the difficulties of achieving this end in disturbed patients. Adequate pre-oxygenation requires at least 2 minutes of 100% oxygen breathing with a close-fitting facemask,[1] which is virtually impossible to achieve in patients who present for ECT. We anticipate that it would be strongly resisted by the psychiatrists because of its disturbing effects on these patients. We continue to advocate manual ventilation during the convulsion so that oxygen delivery is maintained during the period of maximal oxygen consumption. Patients at particularly high risk of regurgitation should be managed with full pre-oxygenation and a rapid sequence induction with cricoid pressure.

Leicester General Hospital,
Leicester LE5 4PW

C.D. HANNING
J. LEW
R.J. EASTLEY

Reference

1. RUSSELL GN, SMITH CL, SNOWDON SL, BRYSON THL. Pre-oxygenation and the parturient patient. *Anaesthesia* 1987; **42:** 346–51.

Depression, anxiety and chronic pain

The hospital anxiety and depression scale (HAD) was designed as an instrument for the detection and assessment of anxiety and depression in general hospital outpatient clinics.[1] The scale has been used widely in the United Kingdom and abroad and is already available in many languages. A recent study confirmed the validity of the HAD in the general hospital setting.[2]

The prevalence of depressive illness in patients with chronic pain is a controversial subject.[3] It has been suggested that the HAD is a suitable screening instrument for this patient population[4,5] but we were concerned about its validity, since positive answers for certain questions might be influenced more by pain than by mood.

We have used the HAD to screen 150 patients with chronic pain of varied aetiology attending a pain relief clinic and 67 patients with advanced cancer in a continuing care unit. The prevalence of morbid depression (a score of 11 or more) in both the pain clinic (28%) and cancer patients (31%) was significantly higher than that reported by Zigmond and Snaith for medical outpatients[1] (13%; Chi-squared test, $p < 0.001$).

We carried out an item analysis of the scale using the combined data from both patient groups. A preliminary analysis showed that the pain clinic and continuing care populations could be combined, since there were no differences between the groups in the mean item score or the pattern of inter-item correlations. The internal consistency of the anxiety and depression subscales was examined by calculating the correlation between the score for each individual question with the total subscale score. Table 1 shows that three questions in the depression scale and two in the anxiety scale had item–total correlations of less than 0.5, although all were still significant ($p < 0.01$). One of these depression questions, D4 ('I feel as if I am slowed down') and the two anxiety questions A4 ('I can sit at ease and feel relaxed') and A6 ('I feel restless as if I have to be on the move') relate to physical activity and comfort, and could be influenced by patients' physical symptoms. However, it is clear that the overall internal reliability of the scale (Cronbach's α) remains high (0.81 for depression and 0.82 for anxiety) and is changed only minimally by removal of individual questions (column 5 in Table 1). The range of item–total correlations (significant at $p < 0.01$) is also comparable with that obtained by Zigmond and Snaith (significant at $p < 0.01$ for anxiety and $p < 0.02$ for depression) in their original validation of this scale.[1]

We therefore believe that the HAD remains an appropriate anxiety and depression rating scale for use in patients with chronic pain, whether malignant or nonmalignant.

Table 1. Analysis of individual questions in the HAD scale.

Question	Mean (SD) score	Item–total correlation	Overall internal reliability coefficient (Cronbach's α)	Internal reliability coefficient with item deleted
Depression scale			0.8081	
D1	1.57 (1.04)	0.615		0.769
D2	0.80 (0.85)	0.599		0.774
D3	0.81 (0.81)	0.646		0.768
D4	2.07 (0.97)	0.43		0.803
D5	0.79 (0.97)	0.40		0.808
D6	1.24 (1.02)	0.72		0.748
D7	0.67 (0.89)	0.43		0.802
Anxiety scale			0.8205	
A1	1.59 (0.98)	0.63		0.785
A2	1.09 (1.07)	0.64		0.783
A3	1.37 (1.06)	0.63		0.784
A4	1.69 (0.92)	0.47		0.811
A5	1.00 (0.88)	0.56		0.797
A6	1.40 (1.01)	0.35		0.832
A7	0.94 (0.90)	0.67		0.779

Pain Clinic,
Leeds General Infirmary,
Leeds LS1 3EX
T.M. Jack
V.A. Walker
Department of Psychiatry,
University of Leeds,
Leeds LS2 9JI
S.J. Morley
Continuing Care Unit,
Royal Marsden Hospital,
London SW3 6JJ
G.W. Hanks
B.M. Finlay-Mills

References

1. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* 1983; **67:** 361–70.
2. Aylard PR, Gooding JH, McKenna PJ, Snaith RP. A validation study of three anxiety and depression self assessment scales. *Journal of Psychosomatic Research* 1987; **31:** 261–8.
3. Romano JM, Turner JA. Chronic pain and depression: does the evidence support a relationship? *Psychological Bulletin* 1985; **97:** 18–34.
4. Clarke IMC, Barnes B. Depression and anxiety in pain clinics. *Anaesthesia* 1986; **41:** 325–6.
5. Charlton JE. Depression and anxiety in pain clinics. *Anaesthesia* 1986; **41:** 875–6.

Pancuronium and renal failure

Dr Smith and his colleagues, in their recent article on prolonged paralysis following an infusion of alcuronium in a patient with renal dysfunction (*Anaesthesia* 1987; **42:** 522–5), described prolonged and profound neuromuscular blockade that lasted for 9 days despite the use of both haemodialysis and haemofiltration. We were recently involved in the care of a patient receiving chronic ambulatory peritoneal dialysis for established renal failure who underwent coronary artery bypass grafts for uncontrolled angina. We planned to ventilate this patient's lungs overnight and also to restart peritoneal dialysis in the immediate postoperative period, and he was therefore given pancuronium to a total dose of 16 mg peroperatively. However, normal neuromuscular function could not be demonstrated using a peripheral nerve stimulator until the third postoperative day, despite the continuation of peritoneal dialysis. There was no evidence of any contributory factors such as metabolic acidosis or liver dysfunction during this period which could have prolonged the neuromuscular blockade.

About 25% of pancuronium is metabolised to 3-hydroxypancuronium, which is half as potent as the parent compound. Both the parent compound and its metabolite are polar hydrophilic substances which would not be expected to cross lipid membranes readily, and this may be the reason why peritoneal dialysis was ineffective in our case.

Despite a previous favourable report of the use of peritoneal dialysis in a patient with renal failure who was given gallamine,[1] our case and that described by Dr Smith confirm that one should not rely upon the use of dialysis to remove from the blood drugs which are known to be excreted slowly in patients with renal disease.

Atracurium does not rely on the kidneys for its excretion so there would seem to be no reason for the use of any other competitive neuromuscular blocking drug in patients with compromised renal function, even in circumstances where a period of postoperative ventilation and/or dialysis is planned.

Bristol Royal Infirmary,
Bristol
W. Sangala
J. Dixon

Reference

1. Lowenstein E, Goldfine C, Flacke WE. Administration of gallamine in the presence of renal failure—reversal of neuromuscular blockade by peritoneal dialysis. *Anesthesiology* 1970; **33:** 556–8.

A reply

It is much safer, I agree, to use atracurium than any other non-depolarising muscle relaxants if good recovery from residual neuromuscular block is desired in patients with compromised renal function who undergo prolonged surgery. It is important that neuromuscular blockade be monitored throughout surgery. This is a very useful routine during anaesthesia for patients in chronic renal failure since it prevents excessive administration of cumulative drugs such as pancuronium. If neuromuscular function was monitored when increments were given, it does indeed suggest that the breakdown product 3-hydroxypancuronium contributed to the persistent block. We have seen a similar effect from an active metabolite during the use of prolonged infusions of vecuronium in patients in renal failure in the intensive therapy unit.[1] Recovery in one patient took 37 hours.

Royal Liverpool Hospital,
P.O. Box 147,
Liverpool L69 3BX
J.M. Hunter

Reference

1. Smith CL, Hunter JM, Jones RS. Vecuronium infusions in patients with renal failure in an ITU. *Anaesthesia* 1987; **42:** 387–93.

The effect of benzodiazepines on evoked potentials

The paper by Dr Loughnan *et al.* (*Anaesthesia* 1987; **42:** 195–8) contained some interesting data on the effect of benzodiazepines on evoked potentials but we feel that their conclusions are too generalised. Somatosensory, auditory and visual stimuli were used to study the early and middle latency components of evoked potentials and since these were not affected by diazepam the investigators concluded that 'relatively large doses of a benzodiazepine can be used without affecting evoked responses'. This conclusion needs to be qualified since our own results have shown a marked benzodiazepine effect on longer latency evoked potentials. In our study, 20 male volunteers randomly allocated to two equal groups received either midazolam 15 mg orally or a placebo in a double-blind manner. Auditory evoked cortical potentials were measured prior to and one hour following tablet administration. The later cortical components (N_{100}, N_{200} and P_{300}) showed a significantly increased latency and decreased amplitude. Figures 1 and 2 show the results from one subject before and after midazolam administration. The placebo group, in contrast, showed no change. Since oral midazolam has a systemic availability of only 41%[1] we do not feel that a 15 mg dose was particularly large and our conclusion is that even moderate doses of benzodiazepines affect cortical auditory evoked potentials. Dr Loughnan's data refer only to the early and middle components of the evoked response and we feel that this should be made clear since their conclusion does not hold for all components.

The Queen's University of Belfast,
Belfast BT9 7BL

K.R. Milligan
R.C. Howard
J.W. Dundee

Reference

1. Greenblatt DJ, Abernethy DR, Looniskar A, Harmatz JS, Limjuco RA, Shader RI. Effect of age, gender and obesity on midazolam kinetics. *Anesthesiology* 1984; **61:** 27–35.

A reply

Thank you for inviting me to reply to the above letter. We do not routinely measure the late cortical components of evoked potentials because of the marked inter-trial variability that occurs. This view is

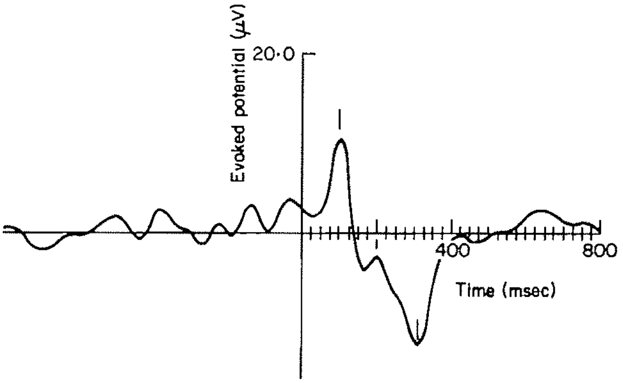


Fig. 1. Auditory evoked response prior to midazolam.

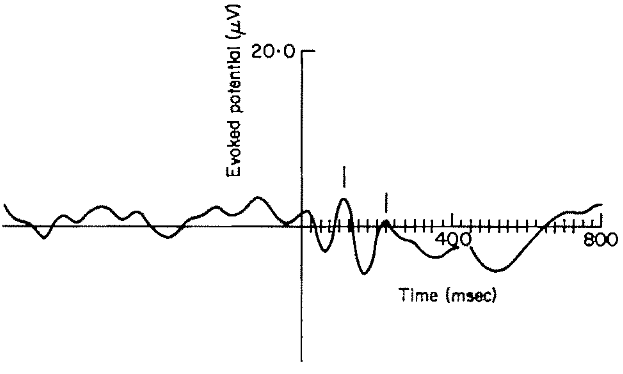


Fig. 2. Evoked responses one hour after oral midazolam 15 mg.

confirmed by Grundy,[1] who also considered the late cortical components too variable to be useful intraoperatively. Indeed, the late cortical components of the auditory evoked response may depend on whether or not the subject is paying attention to the auditory stimulus.[2] Marked changes in the later components of the auditory evoked response undoubtedly do occur with even mild sedation but whether monitoring these components is useful remains doubtful.

The London Hospital,
Whitechapel,
London E1 1BB

P.S. Sebel

References

1. Grundy BL. Intraoperative monitoring of sensory evoked potentials. *Anesthesiology* 1983; **58:** 72–87.
2. Picton TW, Hillyard SA. Human auditory evoked potentials. II. Effects of attention. *Electroencephalography and Clinical Neurophysiology* 1974; **36:** 191–9.

Capnography

This is a report of an unusual incident during anaesthesia which might have resulted in patient awareness if specific monitoring had not been in use.

A fit, middle-aged female had been stabilised in the sitting position for posterior fossa surgery. She was paralysed with relaxants and her lungs ventilated with a Servo 900 ventilator which delivered an $F\text{IO}_2$ of 0.33 in nitrous oxide from a Boyle International Mark 2 anaesthetic machine, with isoflurane 1.5% and fentanyl as supplement. Monitors included an oxygen analyser (no alarm), capnography and a precordial Doppler stethoscope.

The end tidal CO_2 tension decreased before the skin incision by 0.7 kPa (A in Fig. 1). Cardiovascular variables were stable. The breathing system, on first inspection, appeared intact. Then the $F\text{IO}_2$ was noted to be 0.96 with the Rotameters set at 3 and 6 litres/minute of oxygen and nitrous oxide, respectively. The oxygen analyser was disconnected and read 21% in air; reconnected it read 0.96 (B in Fig. 1: two transient increases in CO_2 concentration). The machine was re-examined and the large diathermy/suction apparatus moved so that it no longer compressed the emergency oxygen button that protrudes outside the left-hand edge of the International above the Cardiff swivel. The end tidal CO_2 increased as the $F\text{IO}_2$ decreased to 0.33. An episode of possible awareness was thus avoided. The cause of the decrease in CO_2 tension was confirmed later by repetition at the end of the procedure.

The fundamental absorption band for nitrous oxide is 4.5 μm, similar to that of CO_2 which is 4.3 μm. This overlap and a compounding effect, collision broadening, cause infrared CO_2 analysers to read high in the presence of nitrous oxide.[1] This is overcome by calibrating the analyser in the anaesthetic gas mixture to be used, with the addition of a filter that transmits only the wavelength specific for carbon dioxide. However, thus calibrated, the analyser reads low without nitrous oxide, as demonstrated by this case. The two transient increases (B in Fig. 1) are assumed to be due to slight CO_2 retention or nitrous oxide diffusion, or perhaps both, during the brief periods of disconnexion that occurred when the analyser was checked.

Having only just decided why the capnograph had read low, an episode of true air embolus occurred via an open vein during craniotomy (C in Fig. 1). A degree of discipline was required, therefore, in order to take appropriate action, which was successful and anaesthesia was completed uneventfully.

The only warning given by the Servo 900 of this potential cause of awareness is the hissing of the waste-

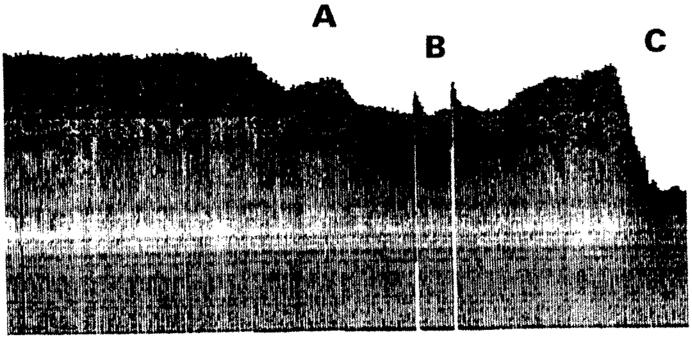


Fig. 1. End-tidal CO_2 tracing.

gate as a result of the high gas flow delivered to it. This was rendered imperceptible by extraneous noise and the Doppler ultrasound. Finally, an alarm function on the oxygen analyser would have hastened diagnosis of the original hazard, that might otherwise have been less rapidly detected without the monitoring in use on this occasion.

The Royal Hallamshire Hospital,
Sheffield S10 2RX
C.M.S. Cooper

Reference

1. Sykes MK, Vickers MD, Hull CJ. *Principles of clinical measurement*, 2nd edn. Oxford: Blackwell Scientific, 1981.

Serological markers for hepatitis B

In 1985 I performed a study on anaesthetists in the Norwich region, similar to that of Sinclair *et al.* (*Anaesthesia* 1987; **42:** 30–2). Of the 42 anaesthetists tested, two (4.8%) were positive for hepatitis B surface antibody. Both had worked for long periods in Africa, in areas where hepatitis B is endemic. No one refused to be tested.

Similar tests were performed on volunteers among those who attended a Norwich anaesthetics study day. All 18 of those tested were negative for surface antibody. This second sample suffers from a similar problem to that of Sinclair, in that some potential subjects opted out.

No samples in my studies or in those of Sinclair were tested for hepatitis B core antibody. This test has the potential to identify previously infected people who are negative for the surface antibody.[1]

However, these figures add to the suggestion of Sinclair *et al.* that anaesthetists do not form a particularly high risk group. In the light of the AIDS epidemic, this may be of some reassurance.

During discussions with those who attended the study day it was of interest to discover the varying attitudes of the different health authorities in the United Kingdom. Many regions offer anaesthetists vaccination against hepatitis B. Others, including the Norwich region, do not.

The Adelaide Children's Hospital,
North Adelaide,
South Australia 5006
G.N. Newcombe

Reference

1. Berry AJ, Isaacson IJ, Kane MA, Schatz GC, Bastron RD, Maze M, Spiss CK, Rizk SF, Ronai AK, Kimovec MA. A multicenter study of the prevalence of hepatitis B viral serologic markers in anesthesia personnel. *Anesthesia and Analgesia* 1984; **63:** 738–42.

An unusual cause of upper airways obstruction

A 23-year-old woman with severe Sturge–Weber syndrome presented as an emergency for oesophagoscopy. The disease was associated with epilepsy and glaucoma as in the original report.[1] Skull X rays in childhood had demonstrated the intracranial calcification initially described by Weber.[2]

Severe mental retardation rendered communication impossible. She had marked gum hypertrophy which developed whilst she received phenytoin between the ages of 6 and 9 years, and continued to progress despite the substitution of phenobarbitone. Bleeding on minimal trauma frequently occurred from these vascular and hypertrophied gums. Management of the concomitant glaucoma had required the administration of a number of general anaesthetics in early childhood but no operative procedures had been undertaken since the hypertrophy of the mucous membranes. The current medication was diazepam, carbamazepine and phenobarbitone.

On examination, the hypertrophic port wine stain was seen to cover most of her face (Fig. 1) with less developed lesions on the back of right arm and several further patches on her legs. The very marked vascular hypertrophy of lips, buccal mucosa, gums and tongue presented an obvious, albeit unusual, anaesthetic hazard.

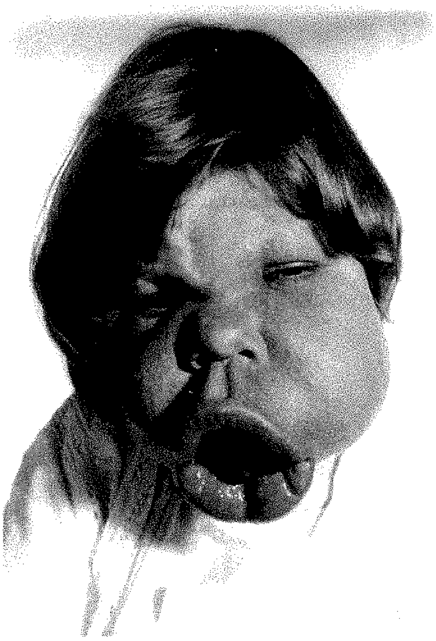


Fig. 1.

Anaesthesia was induced with 50% oxygen in nitrous oxide after intramuscular atropine 0.6 mg, with the patient in the right lateral position to minimise obstruction from her enlarged tongue. Incremental doses of thiopentone and halothane were then given. Maintenance of the airway was difficult and compounded by the inability to achieve an air-tight seal using a variety of facemasks. The markedly enlarged lower lip tended to obstruct the airway despite the use of a large Guedel airway.

The tongue involvement appeared at laryngoscopy to terminate around the posterior third and it was possible to visualise the pharynx and beyond. The larynx appeared normal in vascularity and size so the patient was turned supine and anaesthesia deepened further to insert a long 7-mm cuffed tracheal tube. This tended to kink during the procedure. The lungs were manually ventilated throughout with nitrous oxide, oxygen and halothane. Suxamethonium 75 mg intravenously in divided doses was given to facilitate oesophagoscopy and large pieces of sausage were removed from the lower oesophagus.

On extubation the large tongue and lips again caused airway obstruction and required the insertion of a Guedel airway and considerable mandibular traction until crying commenced when she was able to maintain her own airway.

This patient showed an unusual cause of supralaryngeal upper airways obstruction. Intubation and oesophagoscopy were accomplished without complications despite the grossly hypertrophied vascular tissues and the previous history of haemorrhage on minimal trauma.

Royal Infirmary,
Edinburgh EH3 9YW
L.M. ALDRIDGE

References

1. STURGE WA. A case of partial epilepsy apparently due to a lesion of one of the vaso-motor centres of the brain. *Transactions of the Clinical Society of London* 1879; **12:** 162–7.
2. WEBER FP. Right-sided hemi-hypotrophy resulting from right-sided congenital spastic hemiplegia with a morbid condition of left side of the brain; revealed by radiograms. *Journal of Neurological Psychopathology* 1922; **3:** 134–9.

An improved antipollution device for the Jackson–Rees modification of the Ayre's T-piece

We wish to report a similar device to that described by Dr D.L. Paul (*Anaesthesia* 1987; **42:** 439–40).

The open end of a 3-cm length of the distal end of the casing of a central venous cannula set, such as the Deseret® Angiocath, is fitted directly onto a Portex® swivel connector. The neck of the Dennison valve is inserted through a hole made in the closed end of the clear perspex tube. To achieve a gas-tight fit, the valve is removed from the open end of the bag, which is passed through the hole in the perspex tube and then

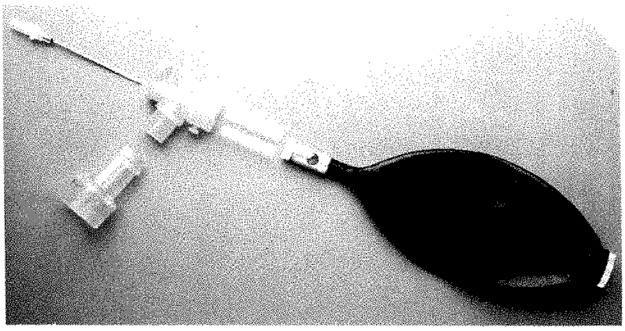


Fig. 1.

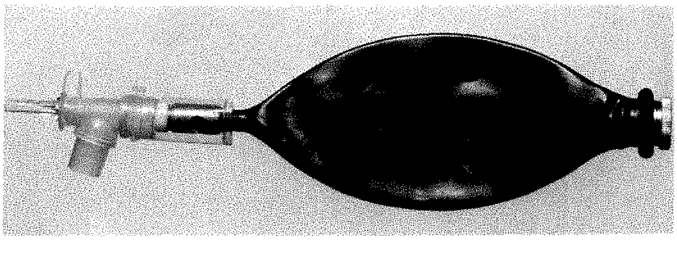


Fig. 2.

re-attached to the valve. The needle of a 14-gauge cannula, with the tip removed, is placed through a hole in the suction port of the swivel connector and fitted snugly into the centre of the Dennison valve (Figs. 1 and 2). The swivel connector attaches via a standard Penlon male adaptor to a passive scavenging system.

This device has been in use for a number of years in this hospital with no untoward sequelae. The total resistance of the system is not increased by the addition of the scavenging device. The advantage of this device over that of Dr Paul is that the Dennison valve can be adjusted easily without opening the system.

Southampton General Hospital,
Southampton SO9 4XY

P.M. Spargo
A. Apadoo
H.J. Wilton

Isoflurane in a drawover anaesthesia system

We should like to comment on the letters from Drs Tighe (*Anaesthesia* 1986; **41:** 1160–1) and Hollis (*Anaesthesia* 1986; **41:** 1161).

We have just completed a clinical trial which compared respiratory variables during halothane and isoflurane anaesthesia in spontaneously breathing patients using the Triservice anaesthetic apparatus.[1] We had thought, like Tighe, that isoflurane might be an ideal agent for use in drawover anaesthesia. However, we found that both induction and maintenance were technically more difficult with isoflurane than with halothane. Our patients were premedicated with pethidine 75–100 mg and atropine 0.6 mg and anaesthesia was induced with thiopentone sodium 300–500 mg. We found, like Hollis, that the more marked respiratory depressant effect[2] and pungency of the isoflurane[3,4] resulted in a slower uptake of the volatile agent.

Induction was prolonged and coughing was a relatively frequent side effect with isoflurane although many of our subjects were heavy smokers. We found maintenance slightly more difficult with isoflurane because there was a tendency for the lightening of anaesthesia with only a small change in vapour concentration. However, we were able to obviate some of the problems of induction with isoflurane by assisting ventilation in the early stages and we produced satisfactory anaesthesia and operating conditions for the shorter cases. Expired carbon dioxide levels are increased and therefore a technique of isoflurane and intermittent positive pressure ventilation with the use of muscle relaxant is more suitable, especially for longer cases.

The use of isoflurane in a drawover anaesthetic apparatus must be the most expensive way to administer it! Furthermore, the maximum output of isoflurane from a Triservice vaporizer is rather greater than 4.0%, which is about three and a half times minimum anaesthetic alveolar concentration (MAC), whereas for halothane a maximum output of 4.5% is six times MAC. The pungency and increased respiratory depression would probably prevent a faster and smoother induction even if it were possible to increase the output of isoflurane.

B.M.H. Munster,
B.F.P.O. 17

S. Yoganathan
I.T. Houghton

References

1. Houghton IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36:** 1094–1108.
2. Fourcade HE, Stevens EC, Larson CP, Cromwell TH, Bahlman SH, Hickey RF, Halsey MJ, Eger EI II. The ventilatory effects of Forane, a new inhaled anesthetic. *Anesthesiology* 1971; **35:** 26–31.
3. Homi J, Konchigeri HN, Eckenhoff JE *et al.* A new anesthetic agent Forane: preliminary observations in man. *Anesthesia and Analgesia* 1972; **51:** 439–77.
4. Pauca AL, Dripps RD. Clinical experience with isoflurane (Forane). *British Journal of Anaesthesia* 1973; **45:** 697–703.

Complications of difficult intubation

The article by Dr Wengen (*Anaesthesia* 1987; **42:** 519–22) was interesting.

It is worth noting that the type of stylet used to assist insertion of the tracheal tube, was not stated. There are several types of stylet available on the market but many are not suitable. Some are short (NCC Satin-Slip stylet, Mallinckrodt) while others are rigid or have a pointed tip (Eschmann Bougie, Eschmann Ltd; plastic coated stylet, Rusch Ltd). The short stylets tend to require repeated attempts at insertion if the tracheal tube initially selected was of unsuitable size. The rigid and pointed stylets tend to cause trauma and may lead to complications.

I have been able to intubate tracheas successfully with the aid of a 14-gauge nasogastric tube when only the epiglottis can be seen at laryngoscopy. The hub of the tube is cut off, the tube is inserted into the pharynx at laryngoscopy and, using a Magill forceps, the tip is guided underneath the epiglottis and into the larynx. The tube is advanced a distance approximately equal to the length of the tracheal tube to be inserted. Suction is applied to the distal end of the tube using a 20-

ml syringe, to ensure that air and not fluid is aspirated. Air is then injected while the abdomen is auscultated to avoid oesophageal intubation.

Thereafter, a tracheal tube of a suitable size is passed over the nasogastric tube into the trachea. If the tracheal tube is too large, it can be replaced by a smaller one without removing the nasogastric tube from the trachea. Nasogastric tubes are longer and softer than the stylets and are therefore easier to manipulate under the epiglottis and hence less traumatic. In addition, a 15-mm tracheal tube connector of a suitable size can be attached to the proximal end which, together with a catheter mount, enables oxygen to be insufflated during attempts at intubation. The nasogastric tube and its connector are kept as part of our difficult intubation box.

Royal Liverpool Hospital,
Liverpool L7 8XP
S.M. Mostafa

AIDS and anaesthesia

It was interesting to read Dr Vella's comments (*Anaesthesia* 1987; **42:** 573). It will not be long before British anaesthetists will follow suit. It should be simple to make the use of gloves a matter of routine in the anaesthetic room and theatre. A time of possibly greater risk is at the resuscitation of cardiac arrest, overdose or trauma victims in casualty where the urgency of the moment may distract from the use of sensible precautions. Anaesthetists involved in these procedures must be encouraged to protect themselves.

Lewisham Hospital,
London SE13 6LH
J.J. Luke
J.M. Cundy

Editor's note

There was an author's error in the letter quoted above. The formula for blood loss should read:

$$\text{Blood loss} = \frac{\text{blood volume}}{\text{starting haematocrit}} \times (\text{starting haematocrit} - 30)$$

Postmortem removal of tracheal tube

The spirit of the recommendations given by Professor Knight and Dr Addicott (*Anaesthesia* 1987; **42:** 554) about the advisability of leaving the tracheal tube in place after a patient has died during a general anaesthetic, for forensic examination is obviously correct but the reasoning is, in my opinion, flawed.

The fixation of a tracheal tube by tying, by adhesive tape or by any other means, cannot guarantee that displacement from the trachea will not occur when the patient is moved from the operating table. It remains standard clinical procedure in most units to recheck the correct position of a tracheal tube after transfer of the anaesthetised patient from the anaesthetic room to the operating table or at any other time when the patient position has been changed, for this very reason, a point made by Dr Watson in his original letter. It is not unknown for a tracheal tube to be displaced during correctly applied external cardiac massage, for example.

Herniation of the cuff of old red rubber tubes across the lumen may, if unrecognised, lead to respiratory obstruction or even death, but herniation is unlikely still be to be present at the time of postmortem examination since the inevitable slow release of gas from the cuffs and the effects of cooling in the refrigerated body will, in my opinion, almost guarantee complete or partial deflation of the cuffs and hence elimination of the obstruction by the time postmortem examination is performed.

It is advisable that the position of the tracheal tube be checked by a second experienced anaesthetist before the body is moved from the operating table should any doubt exist about the cause of death under anaesthesia.

University of Wales
College of Medicine,
Cardiff CF4 4XW
K.R. Johnston

The correspondence about this subject (*Anaesthesia* 1987; **42:** 554) and the legal opinion which was put forward in reply to the reasoned questioning of whether the position of the tracheal tube at postmortem could reliably determine its position during life if the patient died in the course of an operation, was interesting.

Any instrumentation used by doctors on patients may cause injury and, although rare, life-threatening injury can occur from the use of tracheal tubes, for example perforation of the hypopharynx[1] or tracheal rupture.[2] Reports of such cases suggest that death is unusual peroperatively and that initial signs may not always be recognised for their true significance. However, consideration of such problems must imply that, as far as the pathologist is concerned, the cause and effect relationship necessitates that the situation is left as undisturbed as possible. It should also be recognised that if the anaesthetist is aware of any problem, appropriate action may mean that the tube may not remain at the site where the injury occurred. (An example would be unrecognised perforation of the hypopharynx, where failure to expand the lungs was considered to be due to a kinked tube and the tube repositioned.)

Dr Watson's question is obviously about a more thought out problem than whether or not tracheal tubes should remain tied in and cuffs left inflated as the legal opinion seems to imply. An anaesthetist's reputation might be put in some jeopardy when a patient died during surgery where no obvious cause was apparent and it was discovered subsequently at postmortem that the tracheal tube was not in the trachea. Then the question would need to be considered as to whether or not this evidence alone was adequate to explain the cause of death.

All theatre staff are taught about the danger of movement of the patient's head and neck without prior permission from the anaesthetist because of the risks of a disconnexion of the anaesthetic system and also because of the risk of displacement of the tracheal tube. Most anaesthetists are aware of cases where the tube has become displaced during the course of an operation despite this regular discipline. Radiological studies have shown just how much movement of the tracheal tube can occur when the neck is flexed or extended[3] and certainly give grounds for anxiety about displacement when the head and neck are moved about without due care and attention. In addition, the position that the tube takes up when first placed in the trachea tends to vary somewhat as radiological studies in intensive care patients have shown.[4]

If a tube can become displaced under the ideal circumstances of constant supervision by the anaesthetist in the threatre, how much greater will this risk be when such discipline is not exercised? Can portering staff who move the bodies from the theatre reasonably be expected to prevent excessive movement of the head and neck, especially when lifting into and out of all the types of transport trolleys used?

In cases where there is any doubt as to the true location of the tracheal tube in life it should be recognised that this continues to be a difficult problem. If it is assumed that the majority of cases will be associated with difficult intubation where the glottis is not seen at direct laryngoscopy, most of the clinical tests currently used to confirm correct placement have been questioned recently.[5] If the anaesthetist wishes to have objective evidence of the position of the tracheal tube consideration should be given to an X ray of the patient on the operating table prior to moving the body. This has been a means of diagnosing oesophageal intubation in intensive care patients.[6]

Royal Liverpool Hospital, P. Charters
Liverpool L7 8XP

References

1. Lloyd TV, Johnson JC. Infectious cervical spondylitis following traumatic endotracheal intubation. *Spine* 1980; 5: 478–9.
2. Smith BAC, Hopkinson RB. Tracheal rupture during anaesthesia. *Anaesthesia* 1984; 39: 894–8.
3. Conrardy PA, Goodman LR, Laing F, Singer MM. Alteration of endotracheal tube position. Flexion and extension of the neck. *Critical Care Medicine* 1976; 4: 7–12.
4. Goodman LR, Conrardy PA, Laing F, Singer MM. Radiographic evaluation of endotracheal tube position. *American Journal of Roentgenology* 1976; 127: 433–4.
5. Birmingham PK, Cheney FW, Ward RJ. Esophageal intubation: a review of detection techniques. *Anesthesia and Analgesia* 1986; 65: 886–91.
6. Batra AK, Cohn MA. Uneventful prolonged misdiagnosis of esophageal intubation. *Critical Care Medicine* 1983; 11: 763–4.

Difficult tracheal intubation

We encountered difficulty during tracheal intubation of two sisters with testicular feminisation syndrome who were to have laparotomy on the same day for removal of gonadal tissue.

The sisters were 18 and 21 years of age, genetically male but with normal female breasts, no axillary or pubic hair, small vagina and no uterus. They both weighed about 65 kg and did not know of their real genetic status.

Laryngoscopy was easy in the first sister but a Magill red rubber 8-mm internal diameter tracheal tube could not be passed into the trachea. A 6.5-mm internal diameter red rubber tube was eventually passed and was a tight fit. The same problem was expected and experienced when the second sister was anaesthetised; again, a 6.5-mm tube was a tight fit at the level of the cricoid ring. The larynx in both girls had presumably retained its pre-pubertal size and thus would only take a small tracheal tube.

A large literature search failed to find other cases.

Kettering General Hospital, W.F.S. Sellers
Northamptonshire NN16 8UZ S. Yogendran

Anaesthesia, 1987, Volume 42, pages 1244–1245

Book reviews

A History of the Nuffield Department of Anaesthetics, Oxford. 1937–1987 1244
J.M. BEINART
Common Problems in Obstetric Anesthesia 1244
Edited by S. DATTA AND G.W. OSTHEIMER
Infection Control in Intensive Care 1245
Edited by B.F. FARBER
Books received 1245

A History of the Nuffield Department of Anaesthetics, Oxford. 1937–1987

By J. M. BEINART. Pp. 201. Oxford University Press, 1987. £25.00.

This charming book is a good example of the fact that contemporary historians have to learn the language of their subject; Jennifer Beinart is a medical historian of the Wellcome Unit for the History of Medicine and was commissioned to write the history of the first academic department of anaesthetics in the United Kingdom. The publication of her book coincided with the jubilee celebrations of the department.

It is an easy book to read and is equally informative to lay reader and to anaesthetist alike. There are a few lessons on anaesthesia for the uninitiated and instruction in medical and university politics for others. The triumphs and disappointments of this famous department are accorded appropriate emphasis. The former are well known but the endless frustrations which were endured by the founder of that dynasty were, at least to this reader, a revelation. The book is to celebrate a department but it is inevitable and right that a substantial part of it is also a celebration of Professor Sir Robert Macintosh, whom in his ninetieth year, *Anaesthesia* is proud to congratulate.

J.N. LUNN

Common Problems in Obstetric Anesthesia

Edited by S. DATTA AND G.W. OSTHEIMER. Pp. xvi + 496. Year Book Medical Publishers, Inc., 1987. £38.50.

The editors have invited 66 contributors, mainly anaesthetists but including a nurse, a psychologist and a child development research assistant, to address various problems in obstetric anaesthesia. In many chapters two or more authors write about the management of a specific problem from their own particular viewpoint: the chapter on anaesthesia for parturients with diabetes mellitus contains contributions from an obstetrician and an anaesthetist in response to a specific case presentation. There is no mention of the use of continuous insulin infusions in labour, either as a glucose–insulin–potassium solution or via an automatic syringe pump. The chapter on respiratory problems is very short and does not give much practical information to the reader.

The chapter titles occasionally do not reflect accurately the contents: the one on postoperative pain relief is concerned mainly with the management of anaesthesia for elective Caesarean section in a morbidly obese patient. Postoperative analgesia constitutes a very small section and although the importance of pulse oximetry as an indication of respiratory function is emphasised there is no comment on the usefulness of patient-controlled analgesia as well as epidural opioids.

In the preface the editors state that this is not a basic textbook, yet one frequently comes across rather fundamental statements: 'if the patient cannot breathe, then respiratory support is needed'. This is surely obvious and, since it is in relation to the use of magnesium sulphate in the treatment of pre-eclamptic toxaemia and its subsequent interaction with relaxants, may be more appropriate to North American readers.

The index is clear but the reference sections at the end of each chapter are limited with some surprising omissions. There is no reference to the work from Leeds on the use of muscle biopsy in the diagnosis of malignant hyperthermia susceptible patients. Neither is it emphasised that no patient with a family history of susceptibility to malignant hyperthermia should reach the end of a pregnancy without some attempt having been made to exclude the syndrome.

The aims of this textbook are laudable but it will appeal only to a small group of specialist anaesthetists.

It does not in any way replace the excellent available standard textbooks. It may complement these books and perhaps find a place on the shelf of anaesthetic offices in larger maternity units, to be used as a stimulus for discussion of various obstetric anaesthetic problems as they arise.

R. MACDONALD

Infection Control in Intensive Care

Edited by B.F. FARBER. Pp. 214. Churchill Livingstone, 1987. £23.50.

This volume is of importance to all who work in the intensive care unit, irrespective of specialty. All the authors are from North American institutions but the problems which they describe are of universal interest and applicability. Most chapters deal with hospital-acquired infection and its prevention.

The subject of nosocomial infection is introduced by the editor, who draws attention to the fact that, every year, over 2.5 million hospital patients in the United States develop an infection which was neither present nor incubating at the time of admission. The aetiologies, diagnostic features and treatments of pneumonia and bacteraemia are reviewed, and there are chapters on infection in the traumatised patient and the neonate. Indications for isolation in the intensive care unit are discussed in detail. The particular problems of infection in the immunosuppressed patient are described although, inevitably, knowledge about AIDS has increased since the book was written. Urinary tract infections and Legionnaire's disease are discussed in separate chapters. The importance of environmental factors in the spread of infection is stressed in a very detailed and informative chapter, which even considers the efficiency, in respect of reduced bacteria counts, of flushing hospital toilets! The risk of acquired infection to hospital staff is reviewed, as are the mechanisms and prevention of spread of antibiotic resistance.

The importance of infection control programmes is stressed throughout the book. Appropriately, prevention of infection receives a greater emphasis than treatment. Several of the chapters contain an appendix which lists, and grades in order of importance, recommendations for prevention of specific types of infection on the basis of the discussion and review of the literature contained in the preceding pages.

This book is of immense practical value to all hospital staff. It should be compulsory reading for those who work with the critically ill or compromised patient.

A.R. AITKENHEAD

Books received

Acupuncture Treatment and Anaesthesia, 4th edn
By M. SALIM. Pp. 686. The Army Press, Pakistan, 1987. Pakistan Rupees 230.

First Vienna Shock Forum. Parts A and B
Edited by G. SCHLAG AND H. REDL (Progress in Clinical and Biological Research Series, Vols 236A, 236B). Pp. xxv + 664, xxi + 342. Alan R. Liss, Inc., 1987. £59 (Part A), £44 (Part B).

Gastrointestinal Emergencies
Edited by C.W. IMRIE AND A.R. MOOSSA. Pp. 225. Churchill Livingstone, 1987. £25.00.

Recovery Room Care, 2nd edn
By J.S. ISRAEL AND T.J. DEKORNFIELD. Pp. 355. Year Book Publishers, 1987. £34.00.

Anaesthesia, 1987, Volume 42, pages 1246–1254

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for July 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Effect of stress and trauma on bacterial translocation from the gut. Deitch, E.A., Bridges, R.M. *Journal of Surgical Research* 1987; **42:** 536.

Effect of combined blockade of beta-adrenoceptors and acetylcholinesterase in the treatment of post-operative ileus after cholecystectomy. Hallerback, B., Ander, S., Glise, H. *Scandinavian Journal of Gastroenterology* 1987; **22:** 420.

Long-term treatment of irritable bowel syndrome with cimetropium bromide, a new antimuscarinic compound. Piai, G., Visconti, M. *et al. Current Therapeutic Research—Clinical and Experimental* 1987; **41:** 967.

Corticosteroids and intestinal ion transport. Sandle, G.I., Binder, H.J. *Gastroenterology* 1987; **93:** 188.

Acute effects of dexamethasone on cation transport in colonic epithelium. Sandle, G.I., McGlone, F. *Gut* 1987; **28:** 701.

Implications of emergency operations on the colon. Scott-Conner, C.E.H., Scher, K.S. *American Journal of Surgery* 1987; **153:** 535.

Mesenteric and renal responses to stimulation of intestinal receptors by bradykinin. Wever, L., Genovesi, S. *et al. Journal of Hypertension* 1986; **4** (Suppl. 6): S48.

Pharmacology

Adrenergic drugs and their antagonists

Noradrenergic mechanisms in akathisia: treatment with propranolol and clonidine. Adler, L., Angrist, B. *et al. Psychopharmacology Bulletin* 1987; **23:** 21.

A response to isoprenaline unrelated to alpha-/beta-adrenoceptor agonism. Bond, R.A., Clarke, D.E. *British Journal of Pharmacology* 1987; **91:** 683.

Reserpine-induced hypothermia: participation of beta-1 and beta-2 receptors. Frances, H., Simon, P. *Pharmacology, Biochemistry and Behavior* 1987; **27:** 21.

Norepinephrine storage, distribution, and release in diabetic cardiomyopathy. Ganguly, P.K., Beamish, R.E. *et al. American Journal of Physiology* 1987; **252** (Part 1): E734.

Changes in blood flow, portal pressure and shunting during the development of cirrhosis in response to beta-blockade. McLaren, M., Braye, S. *et al. Gut* 1987; **28:** 663.

The effects of simultaneous atropine and labetalol administration on cardiovascular parameters during anticholinesterase poisoning in anaesthetized cat. Merican, Z., Mahmud, Z. *et al. Clinical and Experimental Pharmacology and Physiology* 1987; **14:** 1.

Clinical pharmacokinetics of beta-adrenoceptor antagonists: an update. Riddell, J.G., Harron, D.W.G., Shanks, R.G. *Clinical Pharmacokinetics* 1987; **12:** 305.

Epinephrine increases plasma immunoreactive atrial natriuretic hormone levels in humans. Sanfield, J.A., Shenker, Y. *et al. American Journal of Physiology* 1987; **252** (Part 1): E740.

Modulation of neurotransmitter release by adenosine and ATP. Silinsky, E.M., Ginsborg, B.L., Hirsh, J.K. In: Pelleg, A., ed. *Cardiac electrophysiology and pharmacology of adenosine and ATP*. New York: Alan R. Liss Inc., 1986; p. 65.

Anaesthetic agents

Etomidate inhibits antipyrine metabolism in mice. Atiba, J.O., Blaschke, T.F. *American Journal of the Medical Sciences* 1987; **293:** 361.

Effects of halothane, enflurane and pentobarbital on brain histamine dynamics in mice. Baba, M., Nishibori, M. *et al. Archives of Pharmacology* 1987; **335:** 686.

Effects of phencyclidine and ketamine on cardiovascular activity and temperature in the squirrel monkey. Byrd, L.D. *Life Sciences* 1987; **41:** 7.

Role of isoflurane on hemodynamic properties and disposition of nicardipine. Chelly, J.E., Hysing,

---

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

E.S. *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; **241:** 899.

Effect of atropine on insulin secretion in healthy subjects. Harju, E., Nordback, I. *Journal of International Medical Research* 1987; **15:** 167.

Ro 15-1788 decreases hypnotic effects of sleep deprivation. Lavie, P. *Life Sciences* 1987; **41:** 227.

Differential inotropic effects of halothane and isoflurane in dog ventricular tissues. Luk, H.N., Lin, C.I. *et al. European Journal of Pharmacology* 1987; **136:** 409.

New awakening in anaesthesia—at a price. Leading article. *Lancet* 1987; **1:** 1469.

Collateral blood flow after coronary occlusion—influence of barbiturate anaesthesia and thoracotomy. Melin, J.A., Hutchins, G.M., Becker, L.C. *Cardiovascular Research* 1987; **21:** 416.

Effect of blood transfusion and anesthesia on resistance to bacterial peritonitis. Waymack, J.P., Warden, G.D. *et al. Journal of Surgical Research* 1987; **42:** 528.

Analgesic agents

Effects of morphine on electrical activity of the rectum in man. Bouvier, M., Grimaud, J.C. *Journal of Physiology* 1987; **388:** 153.

The influence of hypothermia on the disposition of fentanyl: human and animal studies. Koren, G., Barker, C. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 373.

Naloxone accelerates the rate of ventilatory acclimatization to hypoxia in awake rats. Olson, E.B. *Life Sciences* 1987; **41:** 161.

Kinetics of morphine in patients with renal failure. Sawe, J., Odarcederlof, I. *European Journal of Clinical Pharmacology* 1987; **32:** 377.

Other drugs

Variations in response to non-steroidal anti-inflammatory drugs. Day, R.O., Brooks, P.M. *British Journal of Clinical Pharmacology* 1987; **23:** 655.

The paradoxical effect of cimetidine and ranitidine on glibenclamide pharmacokinetics and pharmacodynamics. Kubacka, R.T., Antal, E.J., Juhl, R.P. *British Journal of Clinical Pharmacology* 1987; **23:** 743.

5-HT, receptor antagonists: a new class of antiemetics. Leading article. *Lancet* 1987; **1:** 1470.

Pharmacokinetic interactions of cimetidine 1987. Somogyi, A., Muirhead, M. *Clinical Pharmacokinetics* 1987; **12:** 321.

Increased activity of monoamine oxidase by epoxy resin hardeners. Yano, E. *Pharmaceutisch Weekblad* 1987; **9:** 27.

Apparatus

Noninvasive Doppler assessment of human postprandial renal blood flow and cardiac output. Avasthi, P.S., Greene, E.R., Voyles, W.F. *American Journal of Physiology* 1987; **252** (Part 2): F1167.

The oxylog oxygen consumption meter: a portable device for measurement of energy expenditure. McNeil, G., Cox, M.D., Rivers, J.P.W. *American Journal of Clinical Nutrition* 1987; **45:** 1415.

Complications

Cocaine use and the risk for endocarditis in intravenous drug users. Chambers, H.F., Morris, D.L. *et al. Annals of Internal Medicine* 1987; **106:** 833.

Cardiorespiratory arrest and autonomic neuropathy in AIDS. Craddock, C., Pasvol, G. *et al. Lancet* 1987; **2:** 16.

Coronary artery spasm during hydrocortisone-induced allergic reactions. Egashira, K., Origuchi, H. *et al. American Heart Journal* 1987; **113:** 1516.

On the mechanism of the CC14-induced inhibition of liver cytochrome P-450. Ferrali, M., Comporti, M. *Research Communications in Chemical Pathology and Pharmacology* 1987; **56:** 375.

Thrombosed aorta resulting in spinal cord ischemia and paraplegia in ischemic cardiomyopathy. Kochard, G., Kotler, M.N. *et al. American Heart Journal* 1987; **113:** 1510.

Colchicine myopathy and neuropathy. Kuncl, R.W., Duncan, G. *et al. New England Journal of Medicine* 1987; **316:** 1562.

Postoperative cardiac death. Leading article. *Lancet* 1987; **2:** 77.

Orthostatic hypotension due to hypertrophic cardiomyopathy and autonomic failure. Mader, S.L., Wong, M. *American Journal of Medicine* 1987; **82:** 1243.

Mechanisms of liver cell damage in acute hepatitis B. Mohite, B.J., Rath, S. *et al. Journal of Medical Virology* 1987; **22:** 199.

Current concepts: mediators of immediate hypersensitivity reactions. Serafin, W.E., Austen, K.F. *New England Journal of Medicine* 1987; **317:** 30.

Acute pulmonary edema provoked by psychologic stress. Report of two cases. Tavazzi, L., Zotti, A.M., Mazzuero, G. *Cardiology* 1987; **74:** 229.

General anaesthetic procedures

Intravenous midazolam: a study of the degree of oxygen desaturation occurring during upper gastrointestinal endoscopy. Bell, G.D., Reeve, P.A. *et al. British Journal of Clinical Pharmacology* 1987; **23:** 703.

The influence of anesthetic choice on carotid endarterectomy outcome. Corson, J.D., Chang, B.B. *et al. Archives of Surgery* 1987; **122:** 807.

Effects of alfentanil on the pressor and catecholamine responses to tracheal intubation. Crawford, D.C., Fell, D. *et al. British Journal of Anaesthesia* 1987; **59:** 707.

Comparison of local, spinal and general anesthesia for inguinal herniorrhaphy. Young, D.V. *American Journal of Surgery* 1987; **153:** 560.

General interest

Clinical biochemistry of acute hepatic porphyrias. Doss, M. In: Nordmann, Y., ed. *Porphyrins and porphyrias*. Montrouge: John Libbey Eurotext Ltd, 1986; p. 175.

Local autonomic failure affecting a limb. Johnson, R.H., Robinson, B.J. *Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50:** 738.

Pathogenesis of acute porphyria. Moore, M.R., Goldberg, A. *Quarterly Journal of Medicine* 1987; **63:** 377.

The haemolytic uraemic syndrome—a review. Neild, G. *Quarterly Journal of Medicine* 1987; **63:** 367.

Spinal and epidural analgesia

Continuous epidural anesthesia for aortic surgery—thoughts on peer review and safety. Bunt, T.J., Manczuk, M., Varley, K. *Surgery* 1987; **101:** 706.

Spinal opioids

Continuous epidural infusion of morphine for pain relief after cardiac operations. Elbaz, N., Goldin, M. *Journal of Thoracic and Cardiovascular Surgery* 1987; **93:** 878.

Structural requirements for δ opioid receptor binding. Mosberg, H.I., Omnaas, J.R., Goldstein, A. *Molecular Pharmacology* 1987; **31:** 599.

Buprenorphine vs. morphine via the epidural route: a controlled comparative clinical study of respiratory effects and analgesic activity. Pasqualucci, V., Tantucci, C. *et al. Neuroendocrinology* 1987; **46:** 273.

Obstetric anaesthesia and analgesia

A randomized control study of oxytocin augmentation of labour. 1. Obstetric outcome. Bidgood, K.A., Steer, P.J. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 512.

A randomized control study of oxytocin augmentation of labour. 2. Uterine activity. Bidgood, K.A., Steer, P.J. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 518.

Evolving concepts in the mechanism of steroid action: current developments. Faber, L.E., Wakim, N.G., Duhring, J.L. *American Journal of Obstetrics and Gynecology* 1987; **156:** 1449.

Effects of pregnancy on the cytochrome P-450 system in mice. Lambert, G.H., Lietz, H.W., Kotake, A.N. *Biochemical Pharmacology* 1987; **36:** 1965.

Some observations on the effects of a calcium channel blocker—nitrendipine—in early human pregnancy. Lawrence, M.R., Pipkin, F.B. *British Journal of Clinical Pharmacology* 1987; **23:** 683.

Blood coagulation and pregnancy—a review. Newland, J.R. *American Journal of Obstetrics and Gynecology* 1987; **156:** 1420.

Changes in plasma norepinephrine in normal labor following isometric contraction. Rabinovici, J., Rosenthal, T. *et al. Gynecologic and Obstetric Investigation* 1987; **23:** 267.

The influence of pregnancy on drug action: concentration–effect modelling with propranolol. Rubin, P.C., Butters, L. *et al. Clinical Science* 1987; **73:** 47.

Effect of pregnancy on gastric motility *in vivo* and *in vitro* in the guinea pig. Ryan, J.P., Bhojwnal, A., Wang, M.B. *Gastroenterology* 1987; **93:** 29.

Phenytoin infusion in severe pre-eclampsia. Slater, R.M., Wilcox, F.L. *et al. Lancet* 1987; **1:** 1417.

Opioid peptides at term pregnancy in the early puerperium and in postpartum psychosis. Terenius, L., Lyrenas, S. *et al.* In: Nerozzi, D. *et al.*, eds. *Hypothalamic dysfunction in neuropsychiatric disorders*. New York: Raven Press, 1987; p. 201.

Atrial natriuretic peptide concentrations in pre-eclampsia. Thomsen, J.K., Storm, T.L. *et al. British Medical Journal* 1987; **294:** 1508.

Magnesium and pregnancy. Valenzuela, G.J., Munson, L.A. *Magnesium* 1987; **6:** 128.

Paediatric anaesthesia and intensive care

Exaggerated epinephrine responses to hypoglycemia in normal and insulin-dependent diabetic children. Amiel, S.A., Simonson, D.C. *et al. Journal of Pediatrics* 1987; **110:** 832.

Fetal and neonatal effects of the beta-adrenoceptor blocking agents. Boutroy, M.J. *Developmental Pharmacology and Therapeutics* 1987; **10:** 224.

Endogenous opioids modulate fetal rabbit lung maturation. Comer, C.R., Grunstein, J.S. *et al. Journal of Applied Physiology* 1987; **62:** 2141.

The fetal heart insulin receptor responds differently to varying plasma insulin concentrations. Devaskar, S.U., Szewczyk, K., Devaskar, U.P. *Developmental Pharmacology and Therapeutics* 1987; **10:** 153.

Air opening pressure in fetal lungs. Faridy, E.E. *Respiratory Physiology* 1987; **68:** 293.

Rate of secretion of lung surfactant before and after birth. Faridy, E.E., Thliveris, J.A. *Respiration Physiology* 1987; **68:** 269.

Factors influencing mechanical performance of neonatal high-frequency ventilators. Fredberg, J.J., Glass, G.M. *et al. Journal of Applied Physiology* 1987; **62:** 2485.

Cerebral blood flow and brain oxygen extraction in Reye syndrome. Frewen, T.C., Kissoon, N. *Journal of Pediatrics* 1987; **110:** 903.

Severe hypocarbia in preterm infants and neurodevelopmental deficit. Greisen, G., Munck, H., Lou, H. *Acta Paediatrica Scandinavica* 1987; **76:** 401.

Massive transfusion of perfluorocarbon emulsion (fluosal-DA) in newborn piglets. Hall, J.E., Karlson, K.J., Durant, R.H. *Developmental Pharmacology and Therapeutics* 1987; **10:** 163.

Hyponatraemia in premature babies and following surgery in older children. Judd, B.A., Haycock, G.B. *et al. Acta Paediatrica Scandinavica* 1987; **76:** 385.

Continuous transepidermal water loss measurement in sleeping infants. Kahn, A., Rebuffat, E. *et al. Acta Paediatrica Scandinavica* 1987; **76:** 405.

Evaluation of mask-bag ventilation in resuscitation of infants. Kanter, R.K. *American Journal of Diseases of Children* 1987; **141:** 761.

Potassium homeostasis and hypokalemia. Linshaw, M.A. *Pediatric Clinics of North America* 1987; **34:** 649.

Measurement of ventilatory system compliance in infants and young children. Marchal, F., Crance, J.P. *Respiratory Physiology* 1987; **68:** 311.

Effects of fasting and oral premedication on the pH and volume of gastric aspirate in children. Meakin, G., Dingwall, A.E., Addison, G.M. *British Journal of Anaesthesia* 1987; **59:** 678.

Accuracy of blood pressure measurement by the Dinamap monitor in infants and children. Park, M.K., Menard, S.M. *Pediatrics* 1987; **79:** 907.

Post-traumatic central sleep apnea in a child. Querasalva, M.A., Guilleminault, C. *Journal of Pediatrics* 1987; **110:** 906.

Atrial natriuretic peptide in premature and full-term neonates. Rascher, W., Tulassay, T. *et al. Journal of Hypertension* 1986; **4** (Suppl. 6): S506.

Home oxygen therapy in the newborn. Thilo, E.H., Comito, J., McCulliss, D. *American Journal of Diseases of Children* 1987; **141:** 766.

The effect of hematocrit and systolic blood pressure on cerebral blood flow in newborn infants. Younkin, D.P., Reivich, M. *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; **7:** 295.

Cardiovascular system

Physiology

Structure and biologic properties of the atrial natriuretic peptides. Adams, S.P. *Clinics in Endocrinology and Metabolism* 1987; **16:** 1.

Modulation of atrioventricular transmission by adenosine. Belardinelli, L. In: Pelleg, A., ed. *Cardiac electrophysiology and pharmacology of adenosine and ATP.* New York: Alan R. Liss Inc., 1986; p. 109.

Pharmacokinetics of synthetic atrial natriuretic peptides in normal men. Biollaz, J., Callahan, L.T., III *et al. Clinical Pharmacology and Therapeutics* 1987; **41:** 671.

Age-related changes in chest geometry during cardiopulmonary resuscitation. Dean, J.M., Koehler, R.C. *et al. Journal of Applied Physiology* 1987; **62:** 2212.

Relationships between haemodynamic parameters and concentrations of atrial natriuretic peptide in human plasma. Dietz, R., Lang, R.E. *et al. Journal of Hypertension* 1986; 4 (Suppl. 6): S512.

Liver function tests in sickle cell anemia patients—a case control study in Saudi-Arabia. Elhazmi, M.A.F., Alswailem, A.R., Warsy, A.S. *American Journal of the Medical Sciences* 1987; **293:** 371.

The opioid peptides: a role in hypertension. Feuerstein, G., Siren, A. *Hypertension* 1987; **9:** 561.

Cardioselective muscarinic antagonists. Giachetti, A., Mittmann, U. *et al. Federation Proceedings* 1987; **46:** 2523.

Doppler predictions of pulmonary artery pressure, flow, and resistance in adults. Graettinger, W.F., Greene, E.R., Voyles, W.F. *American Heart Journal* 1987; **113:** 1426.

Myotonic dystrophy: ambulatory electrocardiogram, electrophysiologic study, and echocardiographic evaluation. Hiromasa, S., Ikeda, T. *et al. American Heart Journal* 1987; **113:** 1482.

Atrial natriuretic factor receptors. Jacobs, J.W., Vlasuk, G.P., Rosenblatt, M. *Clinics in Endocrinology and Metabolism* 1987; **16:** 63.

Atrial natriuretic peptide is elevated in low-renin essential hypertension. Kiowski, W., Erne, P. *et al. Journal of Hypertension* 1986; 4 (Suppl. 6): S489.

Cardiorespiratory relationships—correlation between the activity of cardio vagus, sympathetic and phrenic nerves. Koizumi, K., Kollai, M. In: Ciriello, J. *et al.*, eds. *Organization of the autonomic nervous system.* New York: Alan R. Liss Inc., 1987; p. 153.

Atrial natriuretic peptide: a new factor in blood pressure control. Lang, R.E., Unger, T., Ganten, D. *Journal of Hypertension* 1987; **5:** 255.

Repolarization abnormalities in mitral valve prolapse. Meyers, D.G., Vallone, N.L., Engel, T.R. *American Heart Journal* 1987; **113:** 1414.

Direct radioimmunoassay of human plasma ANP in various normal and pathophysiological states: increase in renal and cardiac failure during exercise. Morris, M., Cain, M. *et al. Clinical and Experimental Hypertension* 1987; **9:** 703.

Chemical synthesis and structure–activity relations for ANF analogues. Nutt, R.F., Veber, D.F. *Clinics in Endocrinology and Metabolism* 1987; **16:** 19.

Atrial fibrillation: update on mechanism, diagnosis, and management. Olshansky, B., Waldo, A.L. *Modern Concepts of Cardiovascular Disease* 1987; **56:** 23.

The cardiovascular effects of the neurohypophysial hormone oxytocin. PETTY, M.A. *Journal of Autonomic Pharmacology* 1987; **7:** 97.

Increases in oxygen extraction during rapidly fatal septic shock in rats. RACKOW, E.C., ASTIZ, M.E., WEIL, M.H. *Journal of Laboratory and Clinical Medicine* 1987; **109:** 660.

Inhibition of adenosine transport by verapamil and other calcium channel antagonists. ROVETTO, M.J., FORD, D.A. In: PELLEG, A., ed. *Cardiac electrophysiology and pharmacology of adenosine and ATP.* New York: Alan R. Liss Inc., 1986; p. 223.

Changing aspects of the natural history of valvular aortic stenosis. SELZER, A. *New England Journal of Medicine* 1987; **317:** 91.

Effects of acute volume expansion on atrial natriuretic peptide levels in normal subjects, primary aldosteronism and low-renin essential hypertension. TUNNY, T.J., GORDON, R.D. *et al. Journal of Hypertension* 1986; **4** (Suppl. 6): S509.

Platelet catecholamines and platelet function in normal human subjects. WILSON, A.P., SMITH, C.C.T. *et al. Clinical Science* 1987; **73:** 99.

Central alpha 2-adrenergic stimulation increases neurointermediate lobe immunoreactive beta-endorphin in spontaneously hypertensive rats. YASUNARI, K., KANAYAMA, Y. *et al. Hypertension* 1987; **9:** 566.

Treatment and medication

Pharmacology of converting enzyme inhibitors. BRUNNER, H.R., WAEBER, B., NUSSBERGER, J. *Clinical and Experimental Hypertension* 1987; **9:** 275.

Controversies of regimens of thrombolytic therapy in acute pulmonary embolism. CELLA, G., PALLA, A., SASAHARA, A.A. *Seminars in Thrombosis and Hemostasis* 1987; **13:** 163.

Efficacy and influence on quality of life of enalapril as a first step treatment of hypertension. CHATELLIER, G., SASSANO, P. *et al. Clinical and Experimental Hypertension* 1987; **9:** 513.

Effect of pre-operative blood transfusion on tumour metastases. CLARKE, P.J., TARIN, D. *British Journal of Surgery* 1987; **74:** 520.

Hypothermic regional perfusion for protection of the spinal cord during periods of ischemia. COLON, R., FRAZIER, O.H. *et al. Annals of Thoracic Surgery* 1987; **43:** 639.

Mechanism of alpha blockade for blood pressure control. DAVEY, M. *American Journal of Cardiology* 1987; **59:** 18G.

Pharmacokinetic overview of doxazosin. ELLIOTT, H.L., MEREDITH, P.A., REID, J.L. *American Journal of Cardiology* 1987; **59:** 78G.

Acute and subacute hemodynamic effects of enalaprilat, milrinone and combination therapy in rats with chronic left ventricular dysfunction EMMERT, S.E., STABILITO, I.I., SWEET, C.S. *Clinical and Experimental Hypertension* 1987; **9:** 297.

Intravenous labetalol in acute aortic dissection. GRUBB, B.P., SIRIO, C., ZELIS, R. *Journal of the American Medical Association* 1987; **258:** 78.

Efficacy and safety of doxazosin in hypertension therapy. HAYDUK, K. *American Journal of Cardiology* 1987; **59:** 35G.

A differing view of treatment of hypertension in patients with diabetes mellitus. KAPLAN, N.M., ROSENSTOCK, J., RASKIN, P. *Archives of Internal Medicine* 1987; **147:** 1160.

Interactions between magnesium and drugs in the treatment of hypertension. LEARY, W.P. *Magnesium Bulletin* 1987; **9:** 62.

Electrophysiology and antiarrhythmic efficacy of intravenous pirmenol in patients with sustained ventricular tachyarrhythmias. LIEM, L.B., CLAY, D.A. *et al. American Heart Journal* 1987; **113:** 1390.

The metabolic effects of enalapril. MALINI, P.L., STROCCHI, E. *et al. Clinical and Experimental Hypertension* 1987; **9:** 675.

Acute hemodynamic and hormonal effects of CI-930, a new phosphodiesterase inhibitor, in severe congestive heart failure. MURALI, S., URETSKY, B.F. *et al. American Journal of Cardiology* 1987; **59:** 1356.

AIDS and blood transfusion. NAPIER, J.A.F. *British Journal of Anaesthesia* 1987; **59:** 669.

Compensated cardiogenic shock: a subset with damage limited to liver and kidneys. The possible salutary effect of low-dose dopamine. NASCHITZ, J.E., YESHURUN, D. *Cardiology* 1987; **74:** 212.

Side effects and metabolic effects of converting-enzyme inhibitors. NICHOLLS, M.G. *Clinical and Experimental Hypertension* 1987; **9:** 653.

Hemodynamic effects of pirmenol and lidocaine: a placebo-controlled, double-blind, comparative study. NIEMINEN, M.S., TOIVONEN, L. *et al. American Journal of Cardiology* 1987; **59:** 27H.

Side effects and metabolic effects of converting enzyme inhibitors. OMAE, T., KAWANO, Y., YOSHIDA, K. *Clinical and Experimental Hypertension* 1987; **9:** 635.

Drug therapy: nitrate therapy in stable angina pectoris. PARKER, J.O. *New England Journal of Medicine* 1987; **316:** 1635.

Factors affecting the pharmacokinetics of nifedipine. RENWICK, A.G., LEVIE, J. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 351.

Endotoxemia associated with cardiopulmonary bypass. ROCKE, D.A., GAFFIN, S.L. *et al. Thoracic and Cardiovascular Surgery* 1987; **93:** 832.

Clinical orthotopic cardiac transplantation. SALTER, A.D., KLEIN, J.B., GRAY, K.A. *American Journal of Surgery* 1987; **153:** 582.

Indomethacin reduces the antihypertensive action of enalapril. SALVETTI, A., ABDEL-HAQ, B. *et al. Clinical and Experimental Hypertension* 1987; **9:** 559.

Deep vein thrombosis of inferior limbs: are thrombolytic agents superior to heparins? SAMAMA, M.M.

Seminars in Thrombosis and Hemostasis 1987; **13:** 178.

Effect on the endocrine system of a new dopaminergic agent, ibopamine. SORETH, J.T., DUBB, J.W. *et al. Clinical Pharmacology and Therapeutics* 1987; **41:** 627.

Torsade de pointes associated with drugs and toxins: recognition and management. STRATMANN, H.G., KENNEDY, H.L. *American Heart Journal* 1987; **113:** 1470.

Coronary artery disease risk factor management in the hypertensive patient. TAYLOR, S.H. *American Journal of Cardiology* 1987; **59:** 2G.

Calcium antagonists in cerebral/peripheral vascular disorders: current status. TIETZE, K.J., SCHWARTZ, M.L., VLASSES, P.H. *Drugs* 1987; **33:** 531.

Pharmacokinetic and electrophysiologic interactions of amiodarone and procainamidel WINDLE, J., PRYSTOWSKY, E.N. *et al. Clinical Pharmacology and Therapeutics* 1987; **41:** 603.

Life-threatening flecainide toxicity: a pharmacodynamic approach. WINKELMANN, B.R., LEINBERGER, H. *Annals of Internal Medicine* 1987; **106:** 807.

Pharmacologic effects of atrial natriuretic peptide. WINQUIST, R.J. *Clinics in Endocrinology and Metabolism* 1987; **16:** 163.

Respiration

Physiology

Psychophysics—an approach to the study of respiratory sensation and the assessment of dyspnea. ALTOSE, M.D. *American Review of Respiratory Disease* 1987; **135:** 1227.

Ventilatory effectiveness of high-frequency oscillation applied to the body surface. FUYUKI, T., SUZUKI, S. *et al. Journal of Applied Physiology* 1987; **62:** 2410.

Hypoxia-induced changes in shivering and body temperature. GAUTIER, H., BONORA, M. *et al. Journal of Applied Physiology* 1987; **62:** 2477.

Forced expiratory wheezes are a manifestation of airway flow limitation. GAVRIELY, N., KELLY, K.B. *et al. Journal of Applied Physiology* 1987; **62:** 2398.

Electrophysiological and other aspects of excitation–contraction coupling and uncoupling in mammalian airway smooth muscle. GIEMBYCZ, M.A., RODGER, I.W. *Life Sciences* 1987; **41:** 111.

Central neurogenic hyperventilation in a patient with medulloblastoma. GOTTLIEB, D., MICHOWITZ, S.D. *et al. European Neurology* 1987; **27:** 51.

Chemistry and cytotoxicity of reactive oxygen metabolites. GRISHAM, M.B., MCCORD, J.M. In: TAYLOR, A.E. *et al.*, eds. *Physiology of oxygen radicals.* Bethseda, MD: American Physiological Society, 1986; p. 1.

Pulmonary surfactant effects in sublethal hyperoxic lung injury. HOLM, B.A., NOTTER, R.H. In: TAYLOR, A.E. *et al.*, eds. *Physiology of oxygen radicals.* Bethesda, MD: American Physiological Society, 1986; p. 71.

Voluntary breath holding in the obese. HUREWITZ, A.N., SAMPSON, M.G. *Journal of Applied Physiology* 1987; **62:** 2371.

Bronchial mechanical properties and maximal expiratory flows. LAMBERT, R.K. *Journal of Applied Physiology* 1987; **62:** 2426.

Comparison of clinical dyspnea ratings and psychophysical measurements of respiratory sensation in obstructive airway disease. MAHLER, D.A., ROSIELLO, R.A. *et al. American Review of Respiratory Disease* 1987; **135:** 1229.

Alterations in mammalian blood–gas barrier exposed to hyperoxia. MATALON, S., NICKERSON, P.A. In: TAYLOR, A.E. *et al.*, eds. *Physiology of oxygen radicals.* Bethesda, MD: American Physiological Society, 1986; p. 55.

Evidence for individuality of breathing patterns in resting healthy man. SHEA, S.A., WALTER, J. *et al. Respiratory Physiology* 1987; **68:** 331.

The relationship of nonspecific bronchial responsiveness to the occurrence of respiratory symptoms and decreased levels of pulmonary function. SPARROW, D., O'CONNOR, G. *et al. American Review of Respiratory Disease* 1987; **135:** 1255.

Assessment of oxygen radical tissue damage. TAYLOR, A.E., TOWNSLEY, M.I. In: TAYLOR, A.E. *et al.*, eds. *Physiology of oxygen radicals.* Bethesda, MD: American Physiological Society, 1986; p. 19.

Effect of hypoxia-induced periodic breathing on upper airway obstruction during sleep. WARNER, G., SKATRUD, J.B., DEMPSEY, J.A. *Journal of Applied Physiology* 1987; **62:** 2201.

Treatment and medication

Airway response to salbutamol and to ipratropium bromide after non-selective and cardioselective betablocker. DESCHE, P., COURNOT, A. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 343.

High frequency ventilation. FROESE, A.B., BRYAN, A.C. *American Review of Respiratory Disease* 1987; **135:** 1363.

Positive end-expiratory pressure and the damaged right ventricle—an experimental open versus closed chest study. METZLER, H.H., STENZL, W. *et al. Thoracic and Cardiovascular Surgery* 1987; **93:** 823.

Central nervous system

Physiology

Subarachnoid hemorrhage—frequency and severity of cardiac arrhythmias—a survey of 70 cases studied in the acute phase. ANDREOLI, A., DIPASQUALE, G. *et al. Stroke* 1987; **18:** 558.

Late denervation in patients with antecedent paralytic poliomyelitis. Cashman, N.R., Maselli, R. *et al. New England Journal of Medicine* 1987; **317:** 7.

Electrophysiological properties of sympathetic preganglionic neurones *in vivo*. Dembowsky, K., Czachurski, J., Seller, H. In: Cirieus, J. *et al.*, eds. *Organization of the autonomic nervous system.* New York: Alan R. Liss Inc., 1987; p. 3.

Hemorrhagical aspects of the pathophysiology of cerebral ischemia. Gaehtgens, P., Mars, P. *Journal of Cerebral Blood Flow and Metabolism* 1987; **7:** 259.

Role of adrenal catecholamines in cerebrovasodilation evoked from brain stem. Iadecola, C., Lacombe, P.M. *et al. American Journal of Physiology* 1987; **252** (Part 2): H1183.

Effect of hypoxia on traumatic brain injury in rats. Part 1. Changes in neurological function, electroencephalograms and histopathology. Ishige, N., Pitts, L.H., *et al. Neurosurgery* 1987; **20:** 848.

Effect of hypoxia on traumatic brain injury in rats. Part 2. Changes in high energy phosphate metabolism. Ishige, N., Pitts, L.H. *et al. Neurosurgery* 1987; **20:** 854.

Annotation. A unifying conception on the pathogenesis of brain oedemas. Joo, F. *Neuropathology and Applied Neurobiology* 1987; **13:** 161.

Acute stroke, hematocrit, and blood pressure. Larue, L., Alter, M. *et al. Stroke* 1987; **18:** 565.

Disorders of the autonomic nervous system. Part 2. Investigation and treatment. McLeod, J.G., Tuck, R.R. *Annals of Neurology* 1987; **21:** 519.

Atrial natriuretic factor and the central nervous system. Samson, W.K. *Clinics in Endocrinology and Metabolism* 1987; **16:** 145.

Changes in sympatho-adrenal medullary function during aging. Sato, A., Sato, Y., Suzuki, H. In: Ciriello, J. *et al.*, eds. *Organization of the autonomic nervous system.* New York: Alan R. Liss Inc., 1987; p. 27.

Relation of measured brain glucose utilisation and cerebral atrophy in man. Schlageter, N.L., Horwitz, B. *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50:** 779.

Correlations of the severity of autonomic dysfunction to cardiovascular reflexes and to plasma noradrenaline levels in Parkinson's disease. Turkka, J.T. *European Neurology* 1987; **26:** 203.

Agonists and antagonists for excitatory amino acid receptors. Watkins, J.C., Olverman, H.J. *Trends in Neurosciences* 1987; **10:** 265.

Neurotransmitters and memory: role of cholinergic, serotonergic, and noradrenergic systems. Wenk, G., Hughey, D. *et al. Behavioral Neuroscience* 1987; **101:** 325.

Cerebrospinal fluid changes in experimental cardiac arrest (maximal stress). Wortsman, J., Foley, P. *et al. American Journal of Physiology* 1987; **252:** E756.

Treatment and medication

Indomethacin is effective against neurogenic hyperthermia following cranial trauma or brain surgery. Benedek, C., Toth-Daru, P. *et al. Canadian Journal of Neurological Sciences* 1987; **14:** 145.

Diencephalic seizures: responsiveness to bromocriptine and morphine. Bullard, D.E. *Annals of Neurology* 1987; **21:** 609.

The pharmacological management of essential tremor. Findlay, L.J. *Clinical Neuropharmacology* 1986; **9** (Suppl. 2): S61.

The neuroleptic malignant syndrome, so-called—a survey of the world literature. Kellam, A.M.P. *British Journal of Psychiatry* 1987; **150:** 752.

Management of levodopa failures: the use of dopamine agonists. Lieberman, A.N., Gopinathan, G. *et al. Clinical Neuropharmacology* 1986; **9** (Suppl. 2): S9.

[3H] adrenaline release from hypothalamic synaptosomes and its modulation by clonidine: effects of chronic antidepressant drug regimens. McWilliam, J.R., Campbell, I.C. *Life Sciences* 1987; **41:** 145.

Vaiproic acid loading during intensive monitoring. Rosenfeld, W.E., Leppik, I.E. *et al. Archives of Neurology* 1987; **44:** 709.

Parkinson's disease—sensory and motor problems in arms and hands. Schneider, J.S., Diamond, S.G., Markham, C.H. *Neurology* 1987; **37:** 951.

Anticholinergic effects on memory: benztropine *vs.* amantadine. Van Putten, T., Gelenberg, A.J. *Psychopharmacology Bulletin* 1987; **23:** 26.

Endocrine and metabolic

Physiology

Metabolic aspects of the regulation of systemic pH. Atkinson, D.E., Bourke, E. *American Journal of Physiology* 1987; **252** (Part 2): F947.

Human liver microsomal cytochrome-P-450. Beaune P., Ged, C. *et al.* In: Nordmann, Y., ed. *Porphyrins and porphyrias.* Montrouge: John Libbey Eurotext Ltd, 1986; p. 95.

Effect of IV lignocaine on pain and the endocrine metabolic responses after surgery. Birch, K., Jorgensen, J. *et al. British Journal of Anaesthesia* 1987; **59:** 721.

Physiologic and biochemical effects of immobilization on muscle. Booth, F.W. *Clinical Orthopaedics and Related Research* 1987; **219:** 15.

Vasopressin receptors influencing the secretion of ACTH by the rat adenohypophysis. Buckingham, J.C. *Journal of Endocrinology* 1987; **113:** 389.

Anticatabolic effect of human growth hormone in patients treated with glucocorticosteroids. Butenandt, O. In: Laron, Z. *et al.*, eds. *Clinical* *use of growth hormone—present and future aspects.* Basel: S. Karger, 1987; p. 145.

Brain receptors for hypothalamic hormones. Catt, K.J., Millan, M.A. *et al.* In: Nerozzi, D. *et al.*, eds. *Hypothalamic dysfunction in neuropsychiatric disorders.* New York: Raven Press, 1987; p. 51.

Carcinoids and carcinoid syndrome. Creutzfeldt, W., Stockmann, F. *American Journal of Medicine* 1987; **82:** 4.

Vasopressin as vasopressor. Goldsmith, S.R. *American Journal of Medicine* 1987; **82:** 1213.

Effect of methadone on plasma arginine vasopressin level and urine production in conscious dogs. Hellebrekers, L.J., Mol, J.A. *et al. European Journal of Pharmacology* 1987; **136:** 279.

Pancreatic somatostatin is a mediator of glucagon inhibition by hyperglycemia. Klaff, L.J., Taborsky, G.J. *Diabetes* 1987; **36:** 592.

The behavioral physiology of vasopressin and oxytocin. Kovacs, G.L. In: Nerozzi, D. *et al.*, eds. *Hypothalamic dysfunction in neuropsychiatric disorders.* New York: Raven Press, 1987; p. 115.

Fentanyl and the beta-endophin, ACTH and glucoregulatory hormonal response to surgery. Lacoumenta, S., Yeo, T.H. *et al. British Journal of Anaesthesia* 1987; **59:** 713.

Cerebral blood flow increases during insulin-induced hypoglycaemia in type-1 (insulin-dependent) diabetic patients and control subjects. Neil, H.A.W., Gale, E.A.M. *et al. Diabetologia* 1987; **30:** 305.

The clinical significance of inhibition of renal prostaglandin synthesis. Patrono, C., Dunn, M.J. *Kidney International* 1987; **32:** 1.

Beta-endorphin, ACTH, and catecholamine responses in chronic autonomic failure. Polinsky, R.J., Brown, R.T. *et al. Annals of Neurology* 1987; **21:** 573.

Hypothalamic action of atrial natriuretic factor to inhibit vasopressin secretion. Samson, W.K., Aguila, M.C. *et al. Peptides* 1987; **8:** 449.

Effect of vasopressin analogue (dDAVP) on potassium transport in medullary collecting duct. Sonnenberg, H., Honrath, U., Wilson, D.R. *American Journal of Physiology* 1987; **252** (Part 2): F986.

Acute suppression of plasma vasopressin and thirst after drinking in hypernatremic humans. Thompson, C.J., Burd, J.M., Baylis, P.H. *American Journal of Physiology* 1987; **252** (Part 2): R1138.

Metabolic effects of human growth hormone and its possible use in catabolic states. Westphal, O. In: Laron, Z. *et al.*, eds. *Clinical use of growth hormone—present and future aspects.* Basel: S. Karger, 1987; p. 141.

Congenital adrenal hyperplasia. Part II. White, P.C., New, M.I., Dupong, B. *New England Journal of Medicine* 1987; **316:** 1580.

Treatment and medication

Effects of atrial natriuretic factor on the kidney and the renin–angiotensin–aldosterone system. Atlas, S.A., Maack, T. *Clinics in Endocrinology and Metabolism* 1987; **16:** 107.

Bioavailability of bumetanide in grossly oedematous patients. Bailie, G.R., Grennan, A., Waldek, S. *Clinical Pharmacokinetics* 1987; **12:** 440.

Peripheral nerve function in relation to quality of metabolic control in diabetes. Bertelsmann, F.W., Heimans, J.J. *et al. Journal of Neurology* 1987; **234:** 334.

The clinical effects of mixing short and intermediate acting insulins in the treatment of non insulin dependent diabetes. Best, J.D., Ley, C.J. *et al. Medical Journal of Australia* 1987; **146:** 621.

Absence of suppressive effect of somatostatin on prolactin levels in patients with hyperprolactinemia. Bronstein, M.D., Knoepfelmacher, M. *et al. Hormone and Metabolic Research* 1987; **19:** 271.

The relationship between the pharmacokinetics and pharmacodynamic effects of oral hypoglycaemic drugs. Ferner, R.E., Chaplin, S. *Clinical Pharmacokinetics* 1987; **12:** 379.

Low-dose glucose infusion in patients who have undergone surgery: possible cause of muscular energy deficit. Gunther, B., Jauch, K. *et al. Archives of Surgery* 1987; **122:** 765.

Lack of effect of hepatic enzyme induction on metabolic control in patients with type 2 (non-insulin-dependent) diabetes. Korbomen, T., Uusitupa, M. *et al. Clinical Pharmacology and Therapeutics* 1987; **41:** 633.

Effect of antihypertensive treatment on kidney function in diabetic nephropathy. Parving, H., Andersen, A.R. *et al. British Medical Journal* 1987; **294:** 1443.

Outcome of acute cholecystitis in patients with diabetes mellitus. Ransohoff, D.F., Miller, G.L. *et al. Annals of Internal Medicine* 1987; **106:** 829.

Metabolic and immune effects of dietary arginine supplementation after burns. Saito, H., Trocki, O. *et al. Archives of Surgery* 1987; **122:** 784.

Predicting nocturnal hypoglycemia in patients with type 1 diabetes treated with continuous subcutaneous insulin infusion. Schiffrin, A., Suissa, S. *American Journal of Medicine* 1987; **82:** 1127.

Autonomic and peripheral nerve function in early diabetic neuropathy. Possible influence of a novel aldose reductase inhibitor on autonomic function. Sundkvist, G., Lilja, B. *et al. Acta Medica Scandinavica* 1987; **221:** 445.

Massive insulin resistance apparently due to rapid clearance of circulating insulin. Williams, G., Pickup, J.C., Keen, H. *American Journal of Medicine* 1987; **82:** 1247.

Pain

Treatment and medication

The comparative efficacy of naproxen sodium and pirprofen in the treatment of post-operative pain. Baumgartner, H., Kuttelwascher, M. *et al. Journal of International Medical Research* 1987; **15:** 179.

Nalbuphine in patient-controlled analgesia: a comparison with morphine. Christiansen, S. *Current Therapeutic Research—Clinical and Experimental* 1987; **41:** 933.

Cancer pain treatment with a simple custom-built portable waterproof microautoinjector. Yamada, A., Yasoshima, A. *Gynecologic and Obstetric Investigation* 1987; **23:** 275.

Other

Treatment and medication

Influence on oesophageal and gastric emptying and gastro-oesophageal reflux in patients with reflux oesophagitis. Collins, B.J., Spence, R.A.J. *et al. Hepato-Gastroenterology* 1987; **34:** 113.

Safety Information Bulletin

These are issued regularly by the Department of Health and Social Security

Carbon dioxide flow meters on anaesthetic machines: jammed indicator bobbin. SIB(87)4

Bobbins of carbon dioxide flow meters have become wedged at the top of Rotameter tubes due to a combination of a loose footing bobbin stop and a previous user leaving the fine adjustment carbon dioxide valve fully open. Users are reminded of the need for a thorough check of equipment before use.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (UK).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence are to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s), degrees and designations should be typed in lower case below the line. Initials should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction*, *Methods*, *Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left-hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

Use the form of reference adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscripts submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10**: Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article
SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article
ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.
Indicate the approximate position of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ‖, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.
Indicate the approximate position of each figure in relation to the subject matter of the text in the left-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.
All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet
Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS, ABBREVIATIONS AND STATISTICS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 42, no. 11, November 1987

EDITORIAL

The EEG and awareness during anaesthesia
K. Mori 1153

ORIGINAL ARTICLES

Comparison of epidural fentanyl with sufentanil. Analgesia and side effects after a single bolus dose during elective Caesarean section
T.H. Madej and L. Strunin 1156
High frequency ventilation and afferent vagal activity
A.W. Harrop-Griffiths, M.K. Chakrabarti and J.G. Whitwam 1162
Epidural sufentanil versus intramuscular buprenorphine for postoperative analgesia. A double-blind comparative trial
R. Donadoni and G. Rolly 1171
The respiratory depressant effects of nalbuphine and papaveretum as intramuscular premedication
G.G.R. Rutter, W. Aveling and K. Tusiewicz 1176
The effect of rotation of an epidural needle. An *in vitro* study
B.H. Meiklejohn 1180
Subarachnoid block with hyperbaric lignocaine. A comparison with hyperbaric bupivacaine
M.C. Ewart and A.P. Rubin 1183
Tracheal versus intravenous atropine. A comparison of the effects on heart rate
B.M. Bray, H.M. Jones and E.M. Grundy 1188

CASE REPORTS

Hepatotoxicity and death following two enflurane anaesthetics
J.D. Paull and D.W. Fortune 1191
Retrograde intubation. Management of a 4.8-kg, 5-month infant
C.M.S. Cooper and A. Murray-Wilson 1197
Spinal cord compression during chronic epidural morphine administration in a cancer patient
D. van Diejen, J.J. Driessen and J.H.A.M. Kaanders 1201
Large dose epidural sufentanil. Management of postoperative pain with few side effects
T.H. Madej, N.C. Watson and B.C. Martin 1204
Bradycardia during elevation of zygomatic fractures. A variation of the oculocardiac reflex
E.S. Shearer and R. Wenstone 1207
Upper airway obstruction in neurofibromatosis
W.C. Crozier 1209

APPARATUS

Feedback control of neuromuscular blockade. A simple system for infusion of atracurium
C.M. Wait, V.A. Goat and C.E. Blogg 1212

FORUM

Alfentanil infusions. Comparison of bolus administration of fentanyl with three alfentanil infusion regimens
M.E. Stuart-Taylor and J.W. Sleigh 1218
Anaesthetic management for carbon dioxide laser surgery in tracheobronchial lesions
J. Hunton and V.H. Oswal 1222

CORRESPONDENCE 1226

BOOK REVIEWS 1244

ANAESTHETIC LITERATURE 1246

SAFETY INFORMATION BULLETIN 1254

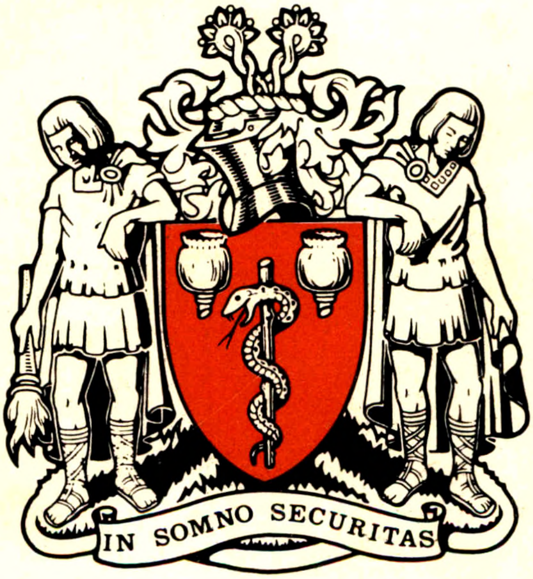
Printed in Great Britain by Richard Clay Ltd, Bungay, Suffolk

6.4.88

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 42 Number 12 December 1987



Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London San Diego New York Berkeley Boston
Sydney Tokyo Toronto

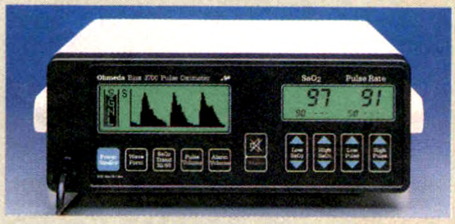
ISSN 0003-2409

Now there's a whole new way to look at pulse oximetry.

Representational r

Ohmeda announces a bright new display.

The Ohmeda Biox 3700 has a bright new LCD that you can really read, three times brighter than before. The panel is easy to see, whether you are standing or sitting, from as far away as 20 feet.



Plus the perfect probe.

The high intensity light source of the new Flex II probe provides a steady, strong signal, able to penetrate variable tissue thickness or pigmentation. Its softer material allows fast, easy application on multiple patient sites. Plus, the economical Flex II is *re-usable* and more flexible, perfect for neonatal and pediatric patients.

Only from Ohmeda—the Company that listens when you talk pulse oximetry.

We're proud to be the original innovators in pulse oximetry. We've been with you from the start—in the OR and in the ICU, in the lab, on your rounds, and in the field for home care. Ohmeda has listened to your ideas and responded to your needs with the exciting new bright display and the revolutionary Flex II *re-usable* probe. And our new software makes the 3700 easy to use on low perfusion patients and during sleep studies.

Proof that Ohmeda puts your best and brightest ideas to work, exactly as you envisioned them.

A new display. A new probe. Both ready for you now.

Your Ohmeda representative has the new 3700 and Flex II re-usable probe ready for delivery. Call us today for your complimentary demonstration. With our field sales and service organization located throughout the world, you'll be looking on the bright side of pulse oximetry right away.

Ohmeda

Ohmeda
Elizabeth Way
Harlow, Essex CM 19 5AB
U.K. Sales Telephone 0279 442001
Telex 81497 OHMEDH G
A Division of The BOC Group Inc.
BOC Health Care

Form #E001 © 1987 The BOC Group Inc

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editor J. N. LUNN
Assistant Editors M. MORGAN, R. GREENBAUM, R. M. JONES, A. R. AITKENHEAD
Editor of *Anaesthesia News* J. N. HORTON
Editorial Board
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
Ex officio
The President of the Association M. ROSEN
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association P. MORRIS
The Immediate Past Honorary Secretary of the Association M. T. INMAN

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. A written statement of this acceptance may be requested by the Editor.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Limited for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
1987, Volume 42, 12 issues. Inland £90.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing.
Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300–0155).
Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
U.S. POSTMASTER: send address changes to "Anaesthesia", c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Second class postage paid at Jamaica, New York 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
© 1987 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.
ISSN 0003–2409

Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
Richard J. Kitz, Emanuel M. Papper, John J. Bonica,
Werner Flacke and A.H. Giesecke, Jr.

Publication: Quarterly
Subscription: Volume 7, 1988
Institutions: £60.00 (UK)/$85.00 (Overseas)

Seminars in Anesthesia will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

From a recent issue

Anesthesia for the Asthmatic Patient, *Ronald Dueck*
Thoracic Anesthesia, *Roger S. Wilson*
Anesthesia for Airway Surgery, *John V. Donlon, Jr*
Anesthesia for the Sickle Cell Diseases and Other Hemoglobinopathies, *Jeff Ray Gibson, Jr*
Anesthesia for Orthopedic Surgery, *Ralph L. Bernstein and Andrew D. Rosenberg*
Clinical Immunology of Chemonucleolysis, *Anna Uitvlugt and Jonathan Moss*
Clinical Aspects of Chemonucleolysis, *Joseph O. Reagan and Howard L. Zauder*
Anesthesia for Extracorporeal Shock Wave Lithotripsy, *David Gissen*

Coupon

Seminars in Anesthesia

To: Journals Marketing Department
Academic Press Ltd
1 Vincent Square
London SW1P 2PN, England

Please tick

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.. Name (Capitals) ....

Address ....

.... Date...........................

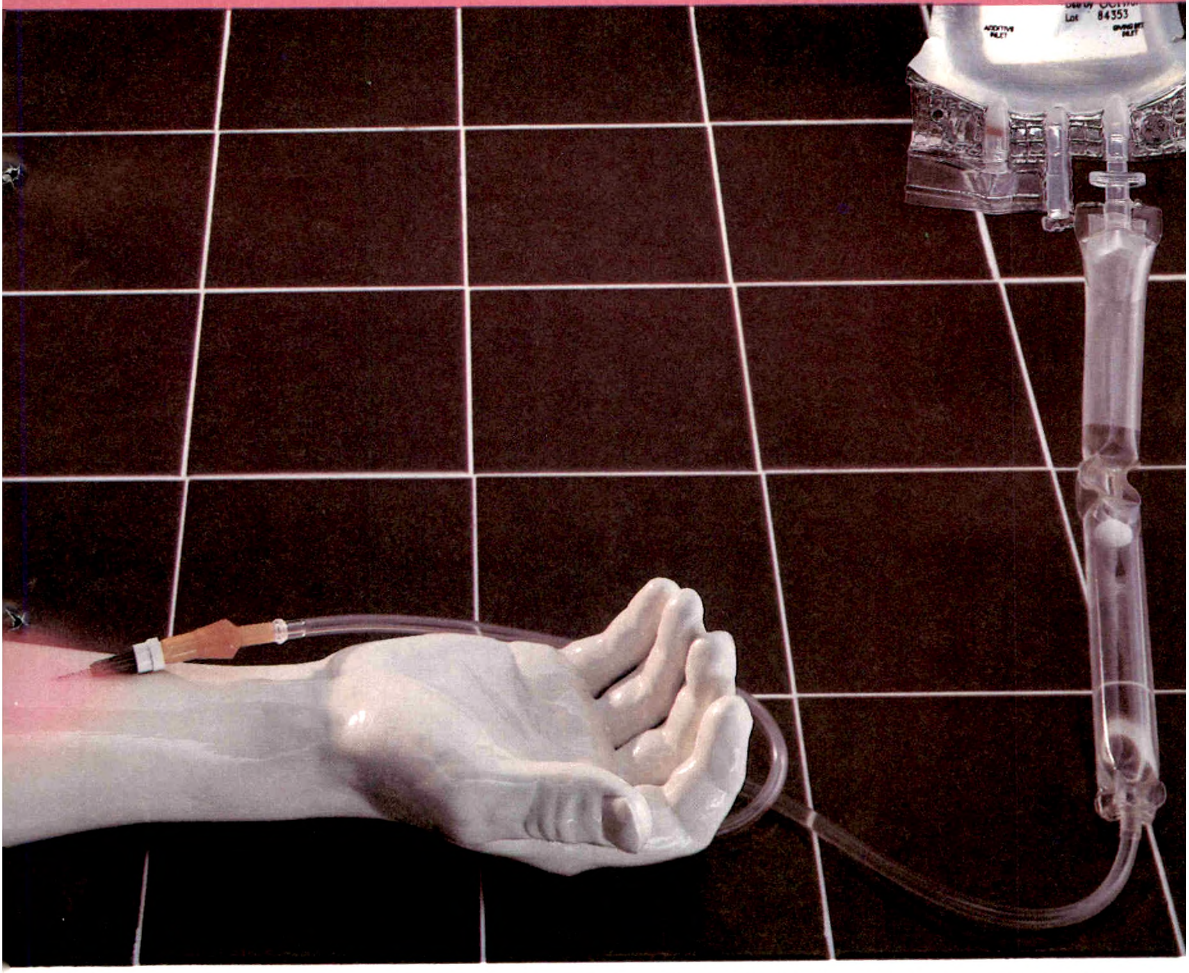
Hespan*
Hetastarch 6%

Controls plasma volume for a full 24 hours

Rapid plasma volume expansion restores cardiac output and tissue perfusion for vital organ function.[1-3]

Reliable increase in colloid osmotic pressure reduces the risk of tissue and pulmonary oedema.[4]

Available freely without dependence on blood donations, without the risk of transmitting disease.



References 1. S. Lazrove, *et al., Crit. Care Med.*, 1980, *8(5)*. **2.** V.K. Puri, *et al.* Data on file. **3.** V. Hempel, *et al., Anaesthetist*, 1975, *24*, 198-201. **4.** M.T. Haupt and E.C. Rackow, *Crit. Care Med.*, 1982, *10*, 159-162. For full prescribing information see next page. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel: (0438) 734549.

DU PONT

*Registered trademark

Hespan Prescribing Information

Composition Each 100ml Hespan contains: Hetastarch 6.0g. Sodium Chloride BP 0.9g. Water for injections BP qs, pH adjusted with Sodium Hydroxide. **Indications** 1. As a plasma volume expander in hypovolaemia. 2. Leucapheresis. 3. Extracorporeal circulation. **Contraindications Warnings** There are no absolute contraindications to the use of Hespan. Use with caution in patients with established renal failure. Hespan can produce dilutional effects on fibrinogen and prothrombin activity. In large volumes, Hespan may alter the coagulation mechanism and produce a transient prolongation of the clotting time. Use with caution in patients with severe bleeding disorders. Use with caution in patients vulnerable to vascular overloading. Caution should be observed before administering Hespan to patients with a history of liver disease in view of slightly raised indirect bilirubin levels observed on very rare occasions in volunteers. There is a low incidence of allergic reactions and the administration is not associated with raised plasma histamine levels. Mild peri-orbital oedema, urticaria or wheezing have been reported and are readily controlled by discontinuation of the drug and, if necessary, administration of an antihistamine. **Dosage and Administration—Plasma Volume Expansion** Intravenous infusion only. In an initial volume approximately equal to half the estimated blood loss. In adults the amount usually administered is 500ml to 1,000ml. Total dosage does not usually exceed 1,500ml per day or 20ml per kg of bodyweight for a typical 70kg patient, however the limiting dose will depend on circulating volume and haematocrit. In acute haemorrhagic shock, an initial administration rate approximately 20ml/kg/hr may be recommended, in burns or septic shock, it is usually administered at slower rates. **Leucapheresis** 250-700ml Hespan is typically added to the Y junction just above the bleed out in the ratio of 1 part citrated Hespan to at least 8 parts whole blood, ratios of 1:20 have been used. On rare occasions, 500ml Hespan has been infused into the donors 15-30 minutes before collection. Multiple leucapheresis procedures using Hespan of up to 2 per week or a total of 7+10 have been reported to be safe and effective. The safety of more frequent or a greater number of procedures has not yet been established. **Product Licence Number** 2737/0042. **Package Quantities** Hespan is supplied in 500ml flexible plastic bags. Basic price £16.72. Distributed for American Hospital Supply by Du Pont (UK) Ltd. For further information contact Du Pont (UK) Ltd., Pharmaceuticals, Wedgwood Way, Stevenage, Herts., SG1 4QN, Tel. (0438) 734549.

DU PONT

New Journal for 1987 . . .

JOURNAL OF CARDIOTHORACIC ANESTHESIA

Editor-in-Chief **Joel A. Kaplan**

Associate Editors
J. Earl Wynands, Cardiac Anesthesia
Roger Wilson, Thoracic Anesthesia
Dennis T. Mangano, Vascular Anesthesia

The Journal of Cardiothoracic Anesthesia is primarily aimed at anesthesiologists dealing with patients undergoing cardiac, thoracic, or vascular surgical procedures. In addition, a multidisciplinary approach will include contributions from cardiac, vascular, and thoracic surgeons, cardiologists, and other internists, intensivists, and related basic scientists. Emphasis will be placed on rapid publication of clinically relevant material applicable to the perioperative period. The purpose of the journal is to consolidate and disseminate original information in these important subspecialties of anesthesiology.

The Journal will publish editorials, original articles, brief clinical studies, large clinical series, case reports, invited state-of-the-art review articles, invited reviews of new drugs and equipment, controversial issues, pertinent abstracts from other journals, letters to the Editor, meeting summaries, news and notes, and book reviews. Innovative submissions using the latest techniques (e.g., two-dimensional color flow doppler and/or computer graphics) will be published at the Journal's expense. In addition, special supplement issues will highlight important topics. The Journal will be international in scope, with submissions encouraged from all continents. Every effort will be made to publish important new information in the shortest possible time. To further this goal of rapid publication in these constantly changing subspecialties, authors will be able to request an "expedited review" of their submissions. A positive "expedited review" will lead to rapid publication for new and controversial material.

Publication: Bi-monthly
Subscription: Volume 1, 1987
Full Rate: $109.00 Overseas / £84.00 (U.K. Only)

For full subscription information and sample copies please apply to Journals Marketing Department at the addresses below.

Grune & Stratton

24–28 OVAL ROAD, LONDON NW1 7DX, UK
ORLANDO, FLORIDA 32887, USA

Free loan of educational video

"The pharmacokinetics of drug infusions"

Written and presented by

PROFESSOR
C J HULL

University of Newcastle-upon-Tyne

Another service to anaesthesia from the Medical Development Department of Janssen.

For details of how to borrow a copy of this video please contact:-

Joanne Hainge,
Anaesthetists Information Service,
Janssen Pharmaceutical Ltd.,
Grove, Wantage, Oxon, UK.
Telephone: 02357 2966

JANSSEN
PHARMACEUTICAL LIMITED

VYGON

Many speak of Seldinger but . . .

VYGON
124
leader cath
Made in France
Cathéter intravasculaire ORX avec guide métallique (méthode de Seldinger) pour la voie sous-clavière
XRO intravascular catheter with metal spring guide (Seldinger-method) for subclavian introduction
VYGON
ECOUEN - FRANCE - Tel.(3) 990.54.55 Telex 695 000 F
B.R.D. - U.K. - BELGIUM - NEDERLAND - ESPANA - EIRE

Seldinger speaks only of Leader-Cath

S. I. Seldinger

Sven-Ivar Seldinger

Vygon (UK) Limited, Bridge Road,
CIRENCESTER, Glos., GL7 1PT.
Telephone: (0285) 67051 Telex: 43342 VYGON G

"Please send me details of the Leader-Cath range"

Name:
Designation:
Hospital:
Address:
Telephone:
Ext:

Anaesthesia with security

Prescribing Information: FORANE* (isoflurane) **Indications:** for inhalation anaesthesia. **Dose:** induction should begin at 0.5% and be adjusted appropriately. Maintenance concentrations generally lie between 1.0% and 2.5%. Elderly: lesser concentrations normally required. Children: adequate data are not available in children under two years of age. **Contraindications:** know sensitivity to Forane, or a history of malignant hyperthermia following a previous adminstration. **Side-effects:** hypotension and respiratory depression. Shivering, nausea and vomiting may occur during recovery. **Basic N.H.S. price:** £33.50 per 100ml. **PL Number:** 0037/0115

Abbott Laboratori
Queenborough, Ken

Anaesthesia, 1987, Volume 42, pages 1255–1257

Editorial

Benzodiazepines

The success of the benzodiazepines since their introduction in the 1960s, has depended on their potency and efficacy as tranquillisers, hypnotics and anticonvulsants and also the huge difference between their therapeutic and fatal doses.[1] The observation in 1973 that desmethyldiazepam could antagonise the reflex depressant effects of diazepam[2] foreshadowed the discovery in 1977 of benzodiazepine (BZ) receptors in the central nervous system (CNS).[3,4] They are located with receptors for γ-aminobutyric acid (GABA), which is the major inhibitory neurotransmitter in the CNS. However, not all GABA receptors contain BZ receptors.

The pharmacological concept of the receptor implies a macromolecule which binds ligands, for example neurotransmitters or drugs, and acts as a transducer to initiate changes in a biological target cell. Benzodiazepines show specific high-affinity receptor binding in the CNS.[5] However, there are also high-affinity binding sites in peripheral organs and in non-neuronal tissues in the CNS, whose function is still unknown.[6] The term 'acceptor' has been proposed for binding sites with no known pharmacological transducer function[7] (e.g. to plasma proteins). The importance of differentiation between true receptor 'versus' high-affinity binding sites was recently reviewed.[8]

The BZ–GABA receptor complex appears to be a tetrameric protein[9–12] that consists of four elongated subunits, 2α and 2β, arranged cylindrically and symmetrically around a chloride channel. The structure of the α and β subunits was recently described.[13] Each of the four subunits in the receptor ($\alpha 2/\beta 2$) contains three domains: a central axial chloride channel domain, outside which is the GABA receptor domain and on which is superimposed the BZ receptor domain. Both GABA and BZ receptors are represented on the cell surface. The main operation of the complex is GABA receptor-mediated gating of the chloride channel, but which can also be modulated allosterically by ligands that act in the other two domains. Conventional benzodiazepine agonists combine with the BZ receptor to change the effect of GABA on the chloride channel, enhancing its effect, so that chloride ions enter the cell to increase its resting membrane potential and hence cause inhibition.[14] Drugs or materials which bind with this system to cause anxiety or convulsions have the opposite effect and are called inverse agonists. The concept of a central physiological anxiety system involved in arousal, which the benzodiazepines antagonise, has led to the hunt for a putative central anxiogenic neurotransmitter. It was thought that β-carbolines might fulfil this role.[15–17] However, in 1983, a unique peptide was described in the central nervous system containing 105 amino acid residues, and which is a powerful inhibitor of the specific receptor binding of diazepam (diazepam binding inhibitor, DBI).[18,19] Its hydrolysis yields an 18-amino-acid fragment which is even more effective in inhibiting diazepam binding (anxiety peptide).[20] However, as yet the existence of such a specific anxiety system and its potential physiological role are not proven.

In addition, partial agonists for both modalities of function have been described, some of which are benzodiazepines and recently a specific BZ receptor antagonist which is also a benzodiazepine, flumazenil (Ro15-1788 or Anexate),[21,22] was developed for clinical use.[23] Thus there are now five groups of ligands for the BZ receptor: agonists, i.e. conventional benzodiazepines; partial agonists (Ro16-6028); inverse agonists, i.e. compounds with anxiogenic and convulsant properties (methyl β-carbolines, DBI, anxiety peptide); partial inverse agonists (these are compounds which, although not convulsant in themselves, facilitate the convulsive properties of other agents such as pentylenetetrazol, for example ethyl β-carbolines, Ro15-4513); and antagonists (flumazenil).

Flumazenil antagonises the effects of all four other groups of ligands. In humans, doses of 100 mg intravenously cause neither agonist nor inverse agonist effects,[24] and it is effective clinically in doses

0003–2409/87/121255 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

of less than 1 mg. It is metabolised to a carboxylic acid derivative (Ro15-3890) which is then glucoronated and excreted. Less than 1% of the drug appears in the urine. It is effective intravenously, orally, intramuscularly and intraperitoneally. Its duration of action following a single dose given intravenously has varied from 15–140 minutes in humans depending on the dose.[25–27] It reverses all the modalities of benzodiazepines but has no effect on their bioavailability or kinetics.[28,29] When anaesthesia is induced with midazolam, by the time the operative procedure has been completed the effects of midazolam are already waning. The administration of flumazenil in the recovery area produces immediate arousal which is sustained since, although the antagonist is short acting, by the time its effects decline the midazolam is also in its terminal pharmacodynamic phase.[27]

Benzodiazepines also inhibit the uptake of adenosine, leading to high extracellular levels which have depressant effects mediated by purinergic receptors; methyl xanthines (e.g. caffeine, theophylline and aminophylline) block purinergic receptors and hence antagonise to a varying extent this action of the benzodiazepines. A large variety of compounds (e.g. cyclopyrrolones, phenylquionolines, triazolopyriadazines, imidazopyridines and peptides) are also ligands for the BZ–GABA receptor complex and hence ready explanations are available for drug interactions as yet to be described.

Concern has been voiced over whether the administration of benzodiazepine antagonists to patients receiving chronic benzodiazepine medication could precipitate an acute abstinence syndrome which can be both serious and prolonged.[30,31] Recent evidence suggests that this concern may be unfounded.[32,33] One concept is that when benzodiazepines are withdrawn, the GABA receptor remains allosterically set in a relatively ineffective configuration and the antagonist could reset the system.[33] One of the problems which complicates studies in patients with benzodiazepine overdose is the development of acute tolerance such that patients may leave hospital with blood levels higher than those at which they were unconscious.[34]

For the future, new powerful pharmacological tools such as monoclonal antibodies may allow discrimination between receptors with different modalities of function and allow mapping of the BZ–GABA systems. New drugs with greater specificity of function will be developed and the already considerable contribution of benzodiazepines to the anaesthetists' armamentarium is likely to increase. The development of flumazenil involved a massive investment of human and material resources. The late entry of this drug into the United Kingdom is to be regretted and could be, at least in part, an indirect consequence of bureaucratic proscription in the 1970s.

Royal Postgraduate Medical School,
London

J. G. WHITWAM

References

1. HAEFELY W, PIERI L, POLC P, SCHAFFNER R. General pharmacology and neuropharmacology of benzodiazepine derivatives. In: HOFFMEISTER F, STILLE G, eds. *Handbook of experimental pharmacology, Vol. 55/II.* Berlin: Springer-Verlag, 1981: 13–262.
2. BARNETT A, FIORE JW. Acute tolerance to diazepam in cats. In: GARATTINI S, MUSSINI E, RANDALL LO, eds. *The benzodiazepines.* New York: Raven Press, 1973: 545–7.
3. MOHLER H, OKADA T. Benzodiazepine receptor: demonstration in the central nervous system. *Science* 1977; **198:** 849–51.
4. BRAESTRUP C, SQUIRES RF. Specific benzodiazepine receptors in rat brain characterized by high-affinity ^{3}H-diazepam binding. *Proceedings of the National Academy of Sciences of the U.S.A.* 1977; **74:** 3805–9.
5. RICHARDS JG, MOHLER H. Benzodiazepine receptors. *Neuropharmacology* 1984; **23:** 233–242.
6. DEL ZOMPO M, BOCCHETTA A, CORSINI GU, TALLMANN JF, GESSA GL. Properties of benzodiazepine binding sites in peripheral tissues. In: BIGGIO G, COSTA E, eds. *Benzodiazepine recognition site ligands: biochemistry and pharmacology.* New York: Raven Press, 1983: 239–48.
7. RICHARDS JG, MOHLER H, HAEFELY W. Benzodiazepine binding sites: receptors or acceptors? *Trends in Pharmacological Science* 1982; **3:** 233–5.
8. LADURON PM. Criteria for receptor sites in binding studies. *Biochemical Pharmacology* 1984; **33:** 833–9.
9. MOHLER H, BATTERSBY MK, RICHARDS JG. Benzodiazepine receptor protein identified and visualized in brain tissue by a photoaffinity label. *Proceedings of the National Academy of Sciences of the U.S.A.* 1980; **77:** 1666–70.
10. THOMAS JW, TALLMAN JF. Characterization of photoaffinity labeling of benzodiazepine binding sites. *Journal of Biological Chemistry* 1981; **256:** 9838–42.

11. Chang LR, Barnard EA. The benzodiazepine/GABA receptor complex: molecular size in brain synaptic membranes and in solution. *Journal of Neurochemistry* 1982; **39:** 1507–18.
12. Karobath M, Supavilai P. Distinction of benzodiazepine agonists from antagonists by photoaffinity labelling of benzodiazepine receptors *in vitro*. *Neuroscience Letters* 1982; **31:** 65–9.
13. Schofield PR, Darlison MG, Fujita N, Burt DR, Stephenson FA, Rodriquez H, Rhee LM, Ramachandran J, Reale V, Glencorse TA, Seeburg PH, Barnard EA. Sequence and functional expression of the GABA receptor shows a ligand-gated receptor super-family. *Nature* 1987; **328:** 221–7.
14. Braestrup C, Nielsen M. Neurotransmitters and CNS disease; anxiety. *Lancet* 1982; **2:** 1030–4.
15. Braestrup C, Nielsen M, Olsen CE. Urinary and brain β-carboline-3-carboxylates as potent inhibitors of brain benzodiazepine receptors. *Proceedings of the National Academy of Sciences of the U.S.A.* 1980; **77:** 2288–92.
16. Braestrup C, Nielsen M. GABA reduces binding of ^{3}H-methyl β-carboline-3-carboxylate to brain benzodiazepine receptors. *Nature* 1981; **294:** 472–4.
17. Braestrup C, Schmiechen R, Neef G, Nielsen M, Petersen EN. Interaction of convulsive ligands with benzodiazepine receptors. *Science* 1982; **216:** 1241–3.
18. Guidotti A, Forchetti CM, Corda MG, Konkel D, Bennett CD, Costa E. Isolation, characterization, and purification to homogeneity of an endogenous polypeptide with agonist action on benzodiazepine receptors. *Proceedings of the National Academy of Sciences of the U.S.A.* 1983; **80:** 3531–35.
19. Editorial. Diazepam binding inhibitor. *Lancet* 1987; **1:** 307–8.
20. Ferrero P, Santi MR, Conti-Tronconi B, Costa E, Guidotti A. Study of an octadeconeuropeptide derived diazepam binding inhibitor (DBI): biological activity and presence in rat brain. *Proceedings of the National Academy of Sciences of the U.S.A.* 1985; **83:** 827–31.
21. Hunkeler W, Mohler H, Pieri L, Polc P, Bonetti EP, Cumin R, Schaffner R, Haefely W. Selective antagonists of benzodiazepines. *Nature* 1981; **290:** 514–6.
22. Prado de Carvalho L, Crecksch G, Chapouthier G, Rossier J. Anxiogenic and non-anxiogenic benzodiazepine antagonists. *Nature* 1983; **301:** 64–6.
23. Kirkegaard L, Knudsen L, Jensen S, Kruse A. Benzodiazepine antagonist Ro15-1788. Antagonism of diazepam sedation in outpatients undergoing cystoscopy. *Anaesthesia* 1986; **41:** 1184–8.
24. Darragh A, Lambe R, Kenny M, Brick I. Tolerance of healthy volunteers to intravenous administration of the benzodiazepine antagonist Ro15-1788. *European Journal of Clinical Pharmacology* 1983; **24:** 569–70.
25. Klotz U, Ziegler G, Reimann IW. Pharmacokinetics of the selective benzodiazepine antagonist Ro15-1788 in man. *European Journal of Pharmacology* 1984; **27:** 115–7.
26. Lauven PM, Schwilden H, Stoeckel H, Greenblatt DJ. The effect of a benzodiazepine antagonist Ro15-1788 in the presence of stable concentrations of midazolam. *Anesthesiology* 1985; **63:** 61–4.
27. Klotz U, Ziegler G, Ludwig L, Reimann IW. Pharmacodynamic interaction between midazolam and a specific benzodiazepine antagonist in humans. *Journal of Clinical Pharmacology* 1985; **25:** 400–6.
28. Darragh A, Lambe R, Kenny M, Brick I, O'Boyle C, Taffe W. Ro15-1788 antagonises the central effects of diazepam in man without altering diazepam bioavailability. *British Journal of Clinical Pharmacology* 1982; **14:** 677–82.
29. O'Boyle C, Lambe R, Darragh A, Taffe W, Brick I, Kenny M. Ro15-1788 antagonises the effects of diazepam in man without affecting its bioavailability. *British Journal of Anaesthesia* 1983; **55:** 349–55.
30. Ashton H. Benzodiazepine withdrawal; an unfinished story. *British Medical Journal* 1984; **288:** 1135–40.
31. Tyner PJ. Benzodiazepine on trial. *British Medical Journal* 1984; **288:** 1101–2.
32. File SE, Baldwin HA. Flumazenil: a possible treatment for benzodiazepine withdrawal anxiety. *Lancet* 1987; **2:** 106–7.
33. Nutt D, Costello M. Flumazenil and benzodiazepine withdrawal. *Lancet* 1987; **2:** 462–3.
34. Greenblatt DJ, Woo E, Allen MD, Orsulak PJ, Schader RI. Rapid recovery from massive diazepam overdose. *Journal of the American Medical Association* 1977; **240:** 1872–4.

Editorial notices

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1:** 432–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1987, Volume 42, pages 1258–1263

Transient hearing loss following spinal anaesthesia

L. P. WANG, J. FOG AND M. BOVE

Summary

Audiograms were performed pre-operatively in 14 patients scheduled for transurethral resection of the prostate under spinal anaesthesia and again 2 days postoperatively. Six of the 14 patients showed a minor reduction of hearing in the low frequency range. Follow-up audiograms showed full recovery after 1–7 months. No significant hearing loss was found in 12 patients who underwent the same procedure with epidural anaesthesia.

Key words

Anaesthetic techniques, regional; spinal, epidural.
Complications; hearing loss
Measurement techniques; audiometry.

The complications of spinal anaesthesia are well recognised and the diagnosis seldom presents problems. Of the late complications, backache and postspinal headache are the most frequent[1–3] although the use of very fine gauge needles has lowered the incidence of the latter.[2,4] Cranial nerve lesions that occur after spinal anaesthesia are usually associated with postspinal headache and both are thought to result from leakage of cerebrospinal fluid (CSF) through the dural puncture.[1–3] Oculomotor, trochlear, abducens, facial and vestibulocochlear nerve lesions have been described.[2,3,5,6] Several recent reports describe hearing loss after spinal anaesthesia[5–7] and it has been suggested that this occurs more often than is generally assumed, although the symptom may be overlooked.[7] The reported incidence of vestibulocochlear nerve involvement after spinal anaesthesia varies between 2‰ and 8%.[3,7]

The aim of this paper is to investigate firstly, the incidence of hearing loss after spinal anaesthesia with bupivacaine in patients who undergo transurethral resection of the prostrate (TURP), secondly, the magnitude of the hearing loss and, thirdly, whether hearing loss is related to postspinal headache.

Methods

Fourteen patients aged 52–73 years scheduled for TURP under spinal anaesthesia were studied with their informed consent. A control group of 12 patients about to have the same operation under epidural anaesthesia was also studied for comparison. Exclusion criteria were systemic disorders apart from arteriosclerosis, history of deafness, cerumen obturans by otoscopy or inability to cooperate with audiometry. The audiological evaluation consisted of pure tone

---

L.P. Wang, MD, Registrar, J. Fog, MD, Consultant, Department of Anaesthesia, M. Bove, MD, Consultant, ENT Department, Eksjö-Nässjö Hospital, S-575 00 Eksjö, Sweden.

0003–2409/87/121263 + 06 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Spinal anaesthesia.

Patient	Age (years)	Needle (gauge)	Bupivacaine (mg)	Pre-operative systolic blood pressure (mmHg)	Maximum decrease in systolic blood pressure (mmHg)	Postoperative headache
1	68	25	17.5	140	15	—
2	60	25	15	135	20	—
3	67	22	15	160	30	yes
4	65	25	17.5	160	30	yes
5	73	25	17.5	120	25	—
6	67	25	15	110	40	—
7	52	25	15	130	30	—
8	71	25	15 + 7.5	130	20	—
9	66	25	13.75	150	25	—
10	59	25	15	180	80	—
11	59	22	15	140	30	—
12	73	22	17.5	160	80	—
13	69	25	15	170	50	—
14	64	25	15	150	20	—
Mean (SD)	65.2 (6.0)		16.2 (2.2)	145 (20)	35 (21)	

Table 2. Epidural anaesthesia.

Patient	Age (years)	Bupivacaine (mg)	Pre-operative systolic blood pressure (mmHg)	Maximum decrease in systolic blood pressure (mmHg)	Postoperative headache
1	53	120	160	50	—
2	75	65	160	110	—
3	70	120	150	20	—
4	75	45	160	0	—
5	61	115	140	50	—
6	69	90	180	40	—
7	67	90	120	10	—
8	69	115	190	30	—
9	69	125	150	65	—
10	56	90	170	30	—
11	68	120	155	15	—
12	68	100	160	40	—
Mean (SD)	66.7 (6.8)	99.6 (24.9)	158 (18)	38 (29)	

audiometry using the ascending technique performed by experienced audiometrists. A Madsen OB70 or OB822 audiometer (Madsen Electronics, Herlev, Denmark) was used and the system was calibrated according to ISO389 (1975). Audiometry was performed in double-walled silent chambers of university clinic standard.

On the morning of the operation an audiogram was performed in each patient who then received premedication according to the preference of the anaesthetist: diazepam 10–15 mg *per rectum*, pethidine 25–50 mg plus dixyrazin 10 mg intramuscularly or morphine 10 mg plus hyoscine 0.4 mg intramuscularly. Spinal anaesthesia was administered in the left lateral position at the third or fourth lumbar interspace following circulatory preloading with 500 ml Ringer's lactate solution. Heavy bupivacaine 0.5% was injected via a 25- or 22-gauge needle. For epidural anaesthesia, plain bupivacaine 0.5% was administered following a test dose of 3 ml via an epidural catheter sited in the third or fourth lumbar interspace.

Systolic arterial blood pressure was measured intermittently during the operation using a sphygmomanometer, and any untoward event recorded. Twelve hours' recumbency was ordered for those patients in whom a 22-gauge spinal needle had been used; posture was unrestricted for the rest of the patients. On the second postoperative day a second audiogram was taken using the same audiometer under the same conditions as the pre-operative examin-

Table 3. Spinal group: change of hearing level (dB), pre- minus postoperative values. Negative values indicate decreased hearing. R, Right ear; L, left ear.

	Frequency (Hz)								
Patient	125	250	500	1000	2000	3000	4000	6000	8000
1 R	−10	−15	−10	−5	−5	0	0	−5	−10
L	−5	0	5	5	−5	−5	0	0	−10
2 R	0	0	0	5	5	0	5	−5	5
L	−5	0	0	0	0	0	−5	−10	0
3 R	−10	−10	−10	−5	−5	0	5	−10	0
L	−15	−15	−15	−5	0	0	0	5	5
4 R	−10	0	0	−5	0	5	5	0	−5
L	−10	−10	−5	0	−5	0	0	0	−5
5 R	0	0	0	0	5	0	0	10	5
L	5	5	0	0	0	5	0	5	0
6 R	5	0	0	0	5	0	−5	15	−5
L	5	0	0	0	0	5	5	15	−10
7 R	5	0	0	0	5	5	5	−5	0
L	−15	−10	5	0	0	0	−5	−5	−5
8 R	0	0	0	0	0	0	0	15	5
L	0	0	0	5	0	0	0	5	0
9 R	−15	−15	−10	0	0	−5	0	−15	−15
L	−10	−15	−15	−5	−5	−5	5	−20	−20
10 R	0	0	0	0	5	0	0	0	0
L	−5	0	−5	0	0	0	−5	0	−5
11 R	10	10	5	0	0	0	0	10	−5
L	0	0	0	5	0	5	0	5	5
12 R	−10	−10	−10	−5	5	−5	0	0	0
L	−15	−10	−15	5	0	0	0	5	0
13 R	5	−5	0	0	0	0	5	−5	10
L	−5	−5	5	0	0	0	0	5	0
14 R	−5	0	−5	0	0	5	0	5	0
L	−5	0	0	−5	5	5	10	5	0

ation. The audiometrist was unaware of the anaesthetic technique employed. Each patient was examined that day by an anaesthetist to elicit symptoms of postspinal headache and evidence of third, fourth, sixth, seventh and eighth cranial nerve palsies.

Patients who had auditory losses of 10 dB or more at two or more adjoining frequencies in either ear postoperatively, were followed up with a third audiogram between 1 and 7 months later.

Calculations and statistical methods. The change of hearing level was calculated at each frequency in each pair of pre- and postoperative audiograms from one patient. In those patients who had a follow-up audiogram, the mean change of hearing level was calculated at each frequency for the group as a whole by comparing the pre-operative and follow-up audiograms. Student's t-test for paired data was used to assess significance at a p value <0.05. Student's t-test for comparison of two independent means was used when results were compared between the two groups. Fisher's exact test was used to compare the numbers of patients in each group who revealed hearing losses of 10 dB or more at two adjoining frequencies in the low frequency range.

Results

There was no difference in the ages of the spinal and epidural groups (mean 65.2 years (SD 6.0) *versus* mean 66.7 years (SD 6.8), $p > 0.05$) (Tables 1 and 2). The mean decrease in systolic arterial blood pressure compared to the pre-operative value in each patient was similar in the spinal and epidural groups (35 mmHg (SD 21) *versus* 38 mmHg (SD 29), $p > 0.05$) and these represented identical changes of 24%. The doses of bupivacaine in the spinal group ranged from 13.75 to 22.5 mg and in the epidural group, from 45 to 125 mg. No evidence of local anaesthetic toxicity was observed and no patient exhibited signs of the TUR syndrome.[8] Two patients in the spinal group developed mild,

Table 4. Epidural group: change of hearing level (dB), pre- minus postoperative values. Negative values indicate decreased hearing. R, Right ear; L, left ear.

Patient	Frequency (Hz) 125	250	500	1000	2000	3000	4000	6000	8000
1 R	−5	−5	0	0	5	0	0	5	−5
L	0	0	0	0	5	0	0	0	10
2 R	5	0	0	0	0	5	5	5	0
L	−5	0	0	5	0	0	0	0	5
3 R	−5	0	0	0	0	0	0	−5	−5
L	0	0	0	0	−5	0	−5	5	−5
4 R	−5	0	0	0	0	0	0	0	0
L	0	−5	0	0	−5	0	5	0	0
5 R	5	5	5	0	5	5	0	0	0
L	0	5	5	0	5	5	5	5	−5
6 R	0	0	0	0	0	5	5	5	−5
L	0	−5	0	0	5	0	0	0	5
7 R	0	5	−5	−5	−5	0	0	0	−5
L	5	0	0	−5	0	0	−5	10	5
8 R	0	0	0	0	0	0	0	5	5
L	0	0	0	0	0	0	0	0	5
9 R	0	0	0	0	0	5	0	−5	5
L	−10	−5	−5	−5	5	0	10	0	0
10 R	5	0	0	0	0	0	5	−5	5
L	0	0	−5	−5	0	0	5	5	5
11 R	5	0	5	0	0	−5	−5	0	0
L	0	0	0	0	−5	−5	0	10	0
12 R	−5	−5	0	0	0	0	5	5	−5
L	0	0	0	0	0	0	0	0	5

Table 5. Spinal group: change of hearing level (dB), pre-operative minus follow-up values in patients who revealed a postoperative hearing loss of 10 dB or more at two or more adjoining frequencies between 125 and 500 Hz. Negative values indicate decreased hearing. Mean hearing loss in each ear is shown at each frequency. R, Right ear; L, left ear.

Patient	Frequency (Hz) 125	250	500	1000	2000	3000	4000	6000	8000
1 R	0	−5	−5	0	0	5	−5	0	−20
L	0	5	5	10	−5	0	−10	0	0
3 R	−5	−5	−10	−5	5	0	−5	−5	−10
L	5	0	−5	0	0	5	5	−5	5
4 R	−5	5	5	0	5	0	5	−5	−5
L	−5	−5	0	−10	−5	−10	−5	−10	5
7 R	10	5	5	5	5	5	5	−10	0
L	−5	−10	5	5	0	0	0	−5	−10
9 R	0	5	0	5	5	0	5	−5	0
L	10	5	0	5	−5	0	10	−5	0
12 R	5	0	−5	5	5	−5	0	5	5
L	−5	−10	−5	5	0	0	0	5	5
Mean*	0.4	−0.8	−0.8	2.1	0.8	0	0.4	−3.3	−2.1

* No significant differences from pre-operative values.

poorly localised headache postoperatively but in neither case was it a typical postspinal headache and both had settled by the following morning. Apart from audiometric changes, no postoperative cranial nerve palsies were detected in either group.

Audiometric results. In the spinal group, six of 14 patients showed hearing losses of 10 dB or more at two or more adjoining frequencies between 125 and 500 Hz (Table 3). This differs significantly ($p < 0.05$) from the observed incidence in the epidural group, in which none of the patients revealed similar hearing losses (Table 4). These six patients showed corresponding increases of hearing level at the follow-up audiograms; that is, their hearing recovered to its pre-operative level (Table 5).

Discussion

The scope of this investigation was, of necessity, limited to the first 2 days postoperatively because of the early discharge of urological patients from this hospital (day 3 onwards). Spinal headache and other neurological sequelae may begin later than 48 hours postoperatively but the onset is earlier in the majority of cases.[2,3] It is possible, therefore, that some minor neurological deficits may have been missed by this study. Audiometric changes may also be delayed for up to 8 days[3] but other studies would suggest that they usually occur within one day of spinal anaesthesia.[5,6] The hearing loss that follows spinal anaesthesia has been attributed to mechanical disturbances due to low intracranial pressure that results from continued leakage of CSF through the dural puncture.[1–3,5,6] No correlations can be made since no true spinal headache occurred in this study.

Although not significant, two of three patients in the spinal group in whom a 22-gauge needle had been employed, revealed postoperative hearing reduction in the low frequency range (cases 3 and 12). Two of the patients in the same group suffered hypotensive episodes in excess of 44% below pre-operative values. In one (case 10) no auditory deficit was noted but in the other (case 12), a marked hearing loss was noted at low frequencies. Further studies of this aspect of regional anaesthesia might suggest an ischaemic aetiology for the auditory deficits. However, a decrease in systolic arterial pressure of 69% was noted without any change of hearing level in one patient (case 2) in the epidural group. No patient revealed any signs of the TUR syndrome[8] and this aetiology does not seem to be a likely factor in the development of postoperative hearing loss.

This study demonstrates that six of 14 patients who had TURP under spinal anaesthesia with bupivacaine revealed hearing losses of 10 dB or more at two or more adjoining frequencies between 125 and 500 Hz. This number differs significantly from the observed zero incidence in the epidural group (12 patients). The finding that the hearing loss was located in the low-frequency area is in accordance with other reports.[5–7] In the present study it was found that patients recovered from their auditory deficits between 1 and 7 months after the operation and this observation is also compatible with several earlier reports.[3,5,7] It is possible that hearing losses after spinal anaesthesia may vary in severity and that only major deficits are associated with other symptoms of decreased CSF pressure, such as postspinal headache. The specific aetiology of disturbances in vestibulocochlear function following spinal anaesthesia is not clear. The decrease in CSF pressure that follows spinal puncture may be transmitted via the cochlear aqueduct, resulting in a corresponding decrease in perilymphatic pressure. This mechanism has been quoted to result in auditory disturbances.[9,10]

This study indicates that hearing loss following spinal anaesthesia with bupivacaine in patients who undergo TURP occurs more often than is generally assumed, although the magnitude may be of minor clinical importance. Furthermore, it is suggested by the follow-up audiograms that the audiometric changes are fully reversible. Minor hearing losses do not seem to be related to the presence of postspinal headache.

Acknowledgments

The authors thank the audiometrists at the ENT Department, Eksjö Hospital, J.E. Wang, statistics student, University of Copenhagen, for statistical advice, Dr J.G. Dalgleish, FFARCS, for assistance in translating the paper into English and the secretaries at the Anaesthetic Department, Eksjö Hospital, for typing and correcting the manuscript.

References

1. BRIDENBAUGH PO, KENNEDY FK. Spinal, subarachnoid blockade. In: COUSINS MJ, BRIDENBAUGH PO, eds. *Neural blockade in clinical anaesthesia and management of pain.* Toronto: Lippincott, 1980: 146–75.
2. VANDAM LD, DRIPPS RD. Long-term follow-up of patients who received 10,098 spinal anaesthetics. Syndrome of decreased intracranial pressure (headache and ocular and auditory difficulties). *Journal of the American Medical Association* 1956; **161:** 586–91.
3. COLLINS VJ. *Principles of anesthesiology.* Philadelphia: Lea and Febiger, 1976: 690–7.

4. Tourtellotte WW, Henderson WG, Tucker RP, Gilland O, Walker JE, Kokman E. A randomized, double-blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post-lumbar puncture syndrome in normal individuals. *Headache* 1972; **12:** 73–8.
5. Wang LP. Sudden bilateral hearing loss after spinal anaesthesia. A case report. *Acta Anaesthesiologica Scandinavica* 1986; **30:** 412–3.
6. Loers FJ. Teilparese des Nervus statoacusticus—eine seltene Komplikation der Spinalanaesthesia. *Anaesthesist* 1977; **26:** 202–3.
7. Panning B, Mehler D, Lehnhardt E. Transient low-frequency hypoacousia after spinal anaesthesia. *Lancet* 1983; **2:** 582.
8. Marx GF, Orkin LR. Complications associated with transurethral surgery. *Anesthesiology* 1962; **23:** 802–13.
9. Arnvig J. Transitory decrease of hearing after lumbar puncture. A personal experience which throws some light on the function of the aqueduct of the cochleae. *Acta Otolaryngologica* 1963; **56:** 699–705.
10. Hughson W. A note on the relationship of cerebrospinal and intralabyrinthine pressures. *American Journal of Physiology* 1932; **101:** 396–407.

Anaesthesia, 1987, Volume 42, pages 1264–1266

Low dose sufentanil pretreatment

Effect on the induction of anaesthesia with thiopentone, methohexitone or midazolam

G. FURNESS, J. W. DUNDEE AND K. R. MILLIGAN

Summary

The effects of pretreatment with varying doses of sufentanil on the subsequent induction of anaesthesia with thiopentone, methohexitone or midazolam were studied in 240 healthy patients. The induction dose requirements for the barbiturates were significantly reduced by sufentanil 5.0 µg (methohexitone $p < 0.05$, *thiopentone* $p < 0.01$*). Excitatory effects following methohexitone were decreased* ($p < 0.01$) *but brief respiratory depression was increased in both cases. Midazolam onset time was reduced, as was the frequency of failed induction, after sufentanil 5.0 µg* ($p < 0.01$)*.*

Key words

Anaesthetics, intravenous; thiopentone, methohexitone.
Analgesics, narcotic; sufentanil.
Hypnotics, benzodiazepines; midazolam.

Methohexitone, of the rapidly acting barbiturate anaesthetic induction agents, causes a high incidence of excitatory phenomena and respiratory upset while thiopentone causes dose-related depression of breathing and arterial blood pressure. Midazolam, the water-soluble benzodiazepine, has been used to induce anaesthesia. It causes minimal cardiorespiratory depression but has a slow and unpredictable onset of action, especially in the young.

Various premedications have been used to ameliorate these problems. Intramuscular morphine and papaveretum decrease the induction dose requirements of thiopentone[1] and reduce the incidence of excitatory effects following methohexitone.[2] Fentanyl and alfentanil given intravenously immediately before induction of anaesthesia, reduce the thiopentone dose requirements and improve the reliability and shorten the onset time with midazolam.[3]

Sufentanil, a synthetic opioid chemically related to fentanyl, has a more rapid onset, shorter duration of action and greater potency than the latter.[4] It has been used as a sole anaesthetic in cardiac anaesthesia[5] but there is no information on the effects of small dosages on the induction of anaesthesia with the barbiturates or midazolam. We here report the influence of pretreatment with sufficiently small doses of sufentanil to maintain spontaneous ventilation, on the action of these three induction agents.

Methods

Following ethical committee approval and clinical trial certificate exemption, three series each

---

G. Furness, FFARCSI, Senior Tutor, J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, K.R. Milligan, FFARCSI, Research Fellow, Department of Anaesthetics, Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

0003–2409/87/121264 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

of 80 fit patients were included in a randomised controlled study to which all had given informed consent. They were scheduled for a variety of operations where the induction agent used was suitable. No premedication was given. The patients were randomly allocated to receive sufentanil 1.0, 2.5 or 5.0 μg intravenously over 2 minutes. Induction of anaesthesia was commenced 2 minutes later using one of the three induction agents. A fourth (control) group received no pretreatment.

When the barbiturates were used, an incremental method (modified from that used in previous studies[1]) was employed with an initial dose (thiopentone 2 mg/kg, methohexitone 0.8 mg/kg) given over 20 seconds into a large antecubital vein followed by increments (thiopentone 25 mg, methohexitone 10 mg) every 15 seconds until loss of verbal contact with the patient occurred. The corresponding induction dose was noted.

With midazolam, a fixed dose of 0.3 mg/kg was given intravenously over 20 seconds and the time to loss of verbal contact with the patient was taken as the induction time. If the patient remained awake at 3 minutes this was deemed a failed induction and anaesthesia was then induced using inhalational agents.

The incidence of respiratory upset (cough, hiccough or laryngospasm) or excitatory phenomena (hypertonus, tremor or involuntary muscle movements) during the induction period was noted, as was any apnoea. Apnoea for longer than 30 seconds was treated by gentle hand ventilation with 66% nitrous oxide in oxygen until adequate spontaneous breathing returned. The incidence of hypotension, taken as a decrease in systolic arterial pressure of more than 40 mmHg or to less than 90 mmHg, was noted.

The results were analysed using analysis of variance, Student's t-test and Chi-squared tests where appropriate.

Results

All groups were broadly comparable with respect to age and weight (Table 1). The sex distribution between the groups was also similar within the thiopentone and methohexitone series but there were more men in the methohexitone group pretreated with sufentanil 5.0 μg. However, when analysis of variance was carried out there was no significant interaction between sex and treatment (F-test, p = 0.82). Consequently, the sex × treatment interaction term was included in the residual error for the test of treatment differences.

Table 1. Demographic data in groups of 20 patients pretreated with varying doses of sufentanil prior to induction with thiopentone or methohexitone. Values expressed as mean (SD).

Sufentanil, μg	Age, years	Weight, kg	Sex, F
Thiopentone groups			
0.0	33 (10)	60 (9)	14
1.0	33 (10)	62 (9)	17
2.5	38 (13)	68 (12)	10
5.0	35 (12)	66 (14)	14
Methohexitone groups			
0.0	33 (12)	63 (11)	16
1.0	33 (11)	60 (10)	15
2.5	37 (12)	67 (15)	18
5.0	35 (12)	68 (10)	10

Table 2 shows that the induction dose for methohexitone was significantly reduced by sufentanil 5.0 μg ($p < 0.05$). A significant reduction in thiopentone dose followed the use of both 2.5 and 5.0 μg sufentanil ($p < 0.01$).

With no pretreatment methohexitone caused a 60% incidence of excitatory effects but these were significantly reduced to 25% or less by 2.5 or 5.0 μg sufentanil ($p < 0.01$). The incidence of brief apnoea at induction was higher in the sufentanil pretreated patients, although the incidence of respiratory upset following this induction agent was not affected. Induction side effects were uncommon following thiopentone. The frequency of respiratory depression at induction was increased by the use of sufentanil but at no time was this a problem clinically.

The induction time following midazolam was significantly reduced by sufentanil 5.0 μg ($p < 0.01$) but not with lower doses. It also significantly reduced the incidence of failed induction (Table 3). Only three patients in this study (two after 5.0 and one after 2.5 μg sufentanil) required manual ventilation for more than one minute. There were no other complications attributable to this drug combination.

Discussion

The findings in this study are similar, with respect to reduction in induction dose of thiopentone and more rapid onset with midazolam, to those found with fentanyl and alfentanil.[3] In

Table 2. Mean induction dose and induction complications following thiopentone or methohexitone in groups of 20 patients pretreated with varying doses of sufentanil or with no pretreatment. Values expressed as mean (SD).

Sufentanil, μg	Barbiturate dosage mg/kg	Barbiturate dosage $\log_e$ (mg/kg)	Induction complications Excitatory phenomena	Induction complications Respiratory upset	Induction complications Apnoea
Thiopentone groups					
0.0	4.4 (1.21)	1.45 (0.29)	0	0	0
1.0	3.9 (0.94)	1.34 (0.23)	0	0	0
2.5	3.2 (0.72)	1.15 (0.23)**	0	0	4
5.0	3.2 (0.78)	1.14 (0.22)**	0	0	11
Methohexitone groups					
0.0	1.4 (0.20)	0.15 (0.07)	12	4	0
1.0	1.5 (0.27)	0.16 (0.08)	8	3	4
2.5	1.4 (0.36)	0.14 (0.11)	5**	8	1
5.0	1.2 (0.29)	0.07 (0.11)*	3**	3	4

* $p < 0.05$, ** $p < 0.01$ *versus* control group.

Table 3. Demographic and midazolam induction data following varying doses of sufentanil or no pretreatment in groups of 20 patients. Values expressed as mean (SD).

Sufentanil, μg	Age, years	Weight, kg	Sex, F	Induction time seconds	Induction time $\log_e$ (seconds)	Induction time <60 seconds	Failed induction†
0.0	34 (8)	61 (8)	18	133 (55)	4.79 (0.49)	2	11
1.0	38 (9)	64 (12)	16	124 (56)	4.60 (0.63)	5	9
2.5	35 (9)	64 (10)	16	118 (60)	4.69 (0.53)	5	8
5.0	32 (11)	61 (10)	14	78 (50)*	4.16 (0.62)*	11*	2*

* $p < 0.01$ *versus* control group.

† Patients not asleep in 180 seconds.

clinical practice, sufentanil has proved ideal for pretreatment prior to barbiturates or midazolam apart from the occurrence of respiratory depression which, for the doses used, was always transient and not of any clinical significance. There were no other side effects associated with its use. The drug is worthy of further study in this field.

Acknowledgment

The authors wish to thank Janssen Pharmaceuticals Ltd for their assistance with this study.

References

1. Dundee JW, Hassard TH, McGowan WAW, Henshaw J. The 'induction' dose of thiopentone. *Anaesthesia* 1982; **37:** 1176–84.
2. Dundee JW, Riding JE, Barron DW, Nichol RM. Some factors influencing the induction characteristics of methohexitone anaesthesia. *British Journal of Anaesthesia* 1961; **33:** 296–302.
3. Dundee JW, Halliday NJ, McMurray TJ, Harper KW. Effect of opioid pretreatment on thiopentone induction requirements and the onset of action of midazolam. *Anaesthesia* 1986; **41:** 159–61.
4. Rosow CE. Sufentanil citrate: a new opioid analgesic for use in anaesthesia. *Pharmacotherapy* 1984; **4:** 11–19.
5. Sebel PS, Bovil JG. Cardiovascular effects of sufentanil anesthesia. *Anesthesia and Analgesia* 1982; **61:** 115–9.

Anaesthesia, 1987, Volume 42, pages 1267–1275

Respiratory depression in children at different end tidal halothane concentrations

S. G. E. LINDAHL, A. P. YATES AND D. J. HATCH

Summary

Respiratory motor function and timing were investigated at end tidal halothane concentrations of 1.5%, 1.0% and 0.5% before and during 4% carbon dioxide stimulation in 10 spontaneously breathing children who weighed between 10.2 and 25.2 kg, during hypospadias repair under halothane anaesthesia. Their tracheas were intubated and all received a caudal block to eliminate surgical stimulation. Pneumotachography and capnography were used and in three cases movements of ribcage and abdomen were also studied by magnetometers. Respiratory drive was evaluated by occlusion tests. Ventilation was depressed at an end tidal halothane concentration of 1.5%, with smaller tidal volumes, higher respiratory rates, higher end tidal carbon dioxide tensions and a weaker respiratory drive compared with 1.0% and 0.5% halothane. Paradoxical breathing was noted at 1.5% as well as at 1.0% but not at 0.5% halothane anaesthesia; the ribcage moved inwards during inspiration. Respiratory compensation during periods of 4% carbon dioxide stimulation was inadequate at 1.5% halothane, as indicated by higher end tidal carbon dioxide tensions, less negative occlusion pressures and movements of ribcage and abdomen that were unresponsive to 4% carbon dioxide, when compared with 1.0% and 0.5% halothane. Respiratory rates were higher and duration of inspiration longer at 1.5% than at 1.0% and 0.5% halothane. Respiratory timing was unaltered by carbon dioxide stimulation. It is concluded that the ventilatory motor response to carbon dioxide is dose dependent and improves at more superficial anaesthetic levels, while respiratory timing is unresponsive to carbon dioxide stimulation irrespective of the halothane concentration used. Paradoxical breathing existed at end tidal halothane concentrations higher than 1%.

Key words

Anaesthesia; paediatric.
Anaesthetics, volatile; halothane.

Breathing is affected differently by various anaesthetic agents[1,2] and respiratory depression by each of the commonly used agents halothane, enflurane and isoflurane is dose dependent.[3–6] The hypoxic ventilatory response is nearly eliminated even at very low concentrations of halothane.[7] It has also recently been shown in young infants, that respiratory timing was unresponsive while motor activity responded to carbon dioxide stimulation when inspired halothane concentrations of about 1% were used.[8] Furthermore, Tusiewicz *et al.*[9] found that at

---

S.G.E. Lindahl,* MD, PhD, A.P. Yates,† MB, BS, FFARCS, D.J. Hatch, MB, BS, FFARCS, Department of Anaesthesia, Hospital for Sick Children, Great Ormond Street, London WC1N 3JN.

* Present address: Department of Anesthesiology, Mayo Clinic, Rochester, MN 55905, USA.

† Present address: Department of Anaesthesia, University College Hospital, Gower Street, London WC1E 6AU.

0003–2409/87/121267 + 09 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

halothane concentrations of 0.8–0.9%, movements of the ribcage did not respond to carbon dioxide stimulation while those of the abdomen did. This suggests that the muscles responsible for movement of the ribcage were more depressed than the diaphragm at this level of halothane anaesthesia. This study did not, however, focus on differences due to various depths of anaesthesia.

The present investigation aimed to quantify respiratory depression in children by comparisons of ventilation, respiratory drive and timing as well as of movements of ribcage and abdomen at three different end tidal halothane concentrations (1.5%, 1.0% and 0.5%) before and during 4% carbon dioxide stimulation.

Methods

Ten spontaneously breathing children, free from cardiorespiratory disease, were fasted for at least 6 hours prior to induction of anaesthesia. Their body weights ranged from 10.2 to 25.2 kg and they were all scheduled for hypospadias repair. Five children were between 1 and 2 years of age and four between 2 and 4 years. One child was 11 years old. Six children who weighed between 10 and 15 kg received pethidine compound 0.07 ml/kg (1 ml contains pethidine 25 mg, promethazine 6.25 mg and chlorpromazine 6.25 mg) with atropine 0.3 mg intramuscularly and the remainder (above 15 kg) had papaveretum 0.4 mg/kg and hyoscine 0.008 mg/kg intramuscularly for premedication 60–90 minutes before induction. Anaesthesia was induced with cyclopropane in oxygen ($F\text{IO}_2$ 0.5) in all children. Intubation of the trachea was facilitated by suxamethonium 1–1.5 mg/kg intravenously and well-fitting Portex tubes were chosen. The children were then allowed to resume spontaneous breathing. Anaesthesia was maintained with oxygen in nitrous oxide ($F\text{IO}_2$ 0.5) and end tidal halothane concentrations of 1.5%, 1.0% and 0.5%. All children received a caudal block with 0.5 ml/kg plain 0.25% bupivacaine after induction of anaesthesia and intubation of the trachea. Routine monitoring in each child consisted of ECG and arterial blood pressure recordings (Dinamap). This study was approved by the hospital ethical committee.

A Mapleson F system was used with fresh gas flows set high enough to avoid rebreathing as indicated by the in-line carbon dioxide meter. In the deadspace of the system was placed the heated head of a Fleisch pneumotachograph No. 0 (linear for flow rates up to 18 litres/minute) and a paediatric cuvette of an in-line capnometer (Hewlett–Packard 14360 A) (Fig. 1). The deadspace of the system measured by water displacement, was 8 ml. Inspiratory and expiratory resistances of the system were 1.4 kPa/litre/second at a flow rate of 10 litres/minute.

Airway pressure was measured at the tube connexion by a pressure transducer (Druck, PDCR-75). The airway occluder was electrically directed (response time 0.03 seconds) by the pneumotachograph so that occlusion occurred precisely when expiration switched to inspiration, namely, at the functional residual capacity (FRC) (Fig. 1). Minute ventilation ($\dot{V}_E$) was measured from tidal volumes (V_T) and respiratory rates (f) after electrical integration of the flow signal. Durations of inspiration (T_I) and of the whole respiratory cycle (T_{tot}) were measured from flow tracings and T_I/T_{tot} ratios were calculated. Mean inspiratory flow (V_T/T_I, ml/second) was also calculated.

In three of the children, weights 12.5, 13.0 and 12.6 kg, movements of ribcage and abdomen were examined. These were measured with midline anteroposterior pairs of magnetometers positioned in the inter-nipple line (ribcage) and 1 cm cranial to the umbilicus (abdomen). Amplification of the magnetometer signals was kept unchanged throughout the study. Flow, volume, end tidal carbon dioxide ($P\text{E}'\text{CO}_2$), pressure and magnetometer signals were recorded on an ink-jet recorder (Siemens–Elema, EM81). Flow and volume calibrations were carried out with an accurate pump which was calibrated against a wet gas meter and the accuracy from repeated measurements was ±0.5%. The capnometer was calibrated with a carbon dioxide tension of 7.73 kPa. The carbon dioxide signal was corrected for the presence of nitrous oxide and for oxygen concentrations. The pressure transducer was calibrated against a pressure of −2.0 kPa.

Three consecutive breathing cycles were followed during airway occlusions, and the time (T_I^o) from the start of an occlusion until the maximal negative airway pressure (P_m^o) was reached, was measured. The exact termination of the occluded breath could not be defined, since there was no gas flow during occlusions. To determine the duration of the whole occluded breath (T_{tot}^o) the time interval between two maximal occlusion

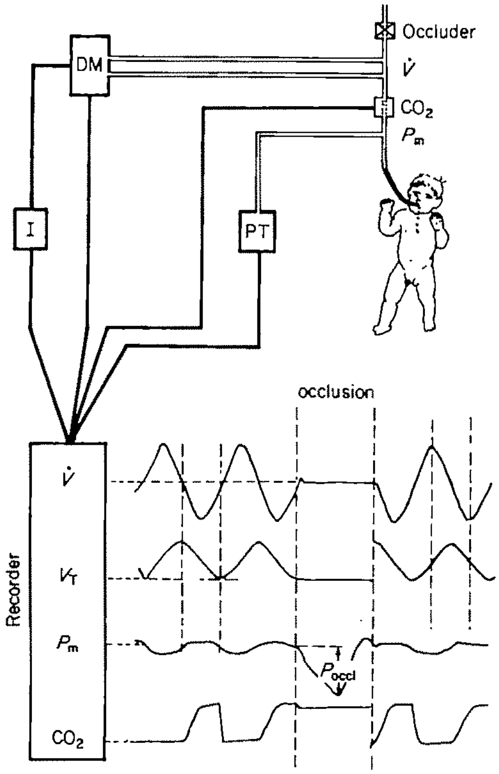


Fig. 1. The apparatus used. P_m, Airway pressure; CO_2, position of the in-line carbon dioxide meter; $\dot{V}$, position of the pneumotachograph. The position of the occluder is also shown. PT, pressure transducer; DM, differential pressure manometer; I, integrator; V_T, tidal volume. Typical tracings are shown and one occlusion breath is given.

pressures was measured. The ratios of inspiration of the occluded breath to its duration (T_I^o/T_{tot}^o) were then calculated. Occlusion pressure curves were biphasic, with an initial fast phase followed by a slower phase. The pressure drop during one second ($\Delta P^o/\Delta t^o$) was measured during both phases.

Measurements of inspired oxygen concentration and of end tidal halothane concentration were carried out intermittently by a sampling multigas analyser (Servo multigas analyser; Siemens–Elema, Stockholm, Sweden). The analyser was calibrated using certified gas mixtures of oxygen and halothane (gas concentrations in cylinders were determined after gravimetric measurements of actual weight and analysis of gas concentrations with a gas chromatograph, with a precision of ±0.01%). Measured signals from the gas analyser were recorded on the ink-jet recorder. Intermittent use of the analyser was chosen in order to keep the volume of the added apparatus deadspace to a minimum and avoid interference with volume measurements. During the 5-minute periods of 4% carbon dioxide stimulation, carbon dioxide was added to the anaesthetic gases from carbon dioxide Rotameters without changing the setting of the oxygen and nitrous oxide Rotameters or the halothane vaporizer.

Procedure

Measurements were performed at 1.5% halothane followed by 1.0% and 0.5% in all children. A reverse order of halothane concentrations was not used, in order not to prolong the recovery period.

Inspired halothane concentrations were set to give an end tidal halothane concentration of 1.5% after the trachea was intubated and caudal analgesia established. Variations in end tidal halothane concentrations were noted to be small after 30 minutes; no measurements were performed in these first 30 minutes. The operation had usually commenced during this period but measurements were not taken precisely at the start of surgery. Measurements were made first for carbon-dioxide-free breathing followed by 5 minutes of 4% carbon dioxide breathing. The end tidal halothane concentration was then reduced to 1.0% and a 30-minute stabilisation period followed before the next measurements were performed. Finally, a stable end tidal halothane concentration of 0.5% was established and another 30-minute period elapsed before the measurements were repeated.

Statistics

Mean values, standard deviations (SD) and standard errors of the mean (SEM) were calculated. Variance analysis of the data was performed for the various concentrations of halothane and the results before and during carbon dioxide stimulation were evaluated by paired two-tailed *t*-tests. Probability values below 0.05 were considered to indicate statistical significance. Mean values (SEM) are presented.

Results

There were no changes in arterial blood pressure or heart rate at the start of surgery in any child,

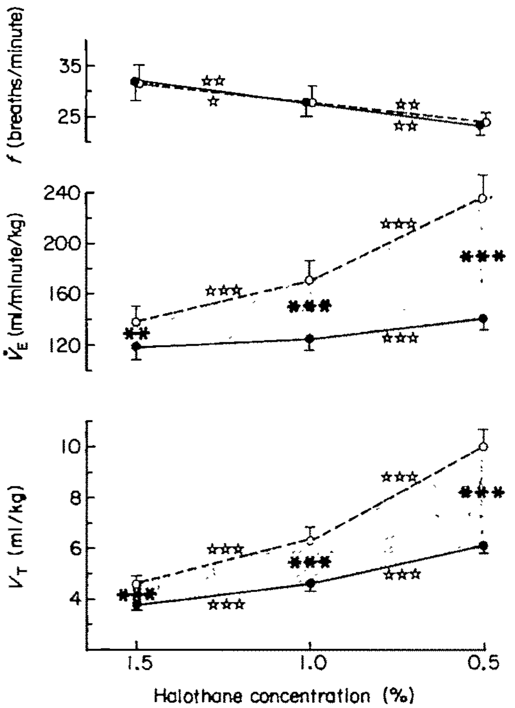


Fig. 2. Mean values (SEM) of tidal volume (V_T), minute ventilation ($\dot{V}_E$) and respiratory rate (f) at 1.5%, 1.0% and 0.5% halothane before (filled circles) and during 4% carbon dioxide breathing (open circles). $^{**}p < 0.01$, $^{***}p < 0.001$ for differences between measurements before and during carbon dioxide breathing. $^{☆}p < 0.05$, $^{☆☆}p < 0.01$, $^{☆☆☆}p < 0.001$ for differences between 1.5% and 1.0% as well as between 1.0% and 0.5% halothane.

which indicates an effective caudal block. Mean arterial blood pressure (MAP) was similar at the various halothane concentrations before as well as during 4% carbon dioxide stimulation. Measured variables changed in the same direction irrespective of the premedication used.

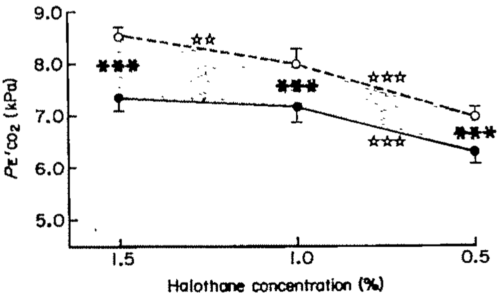


Fig. 3. Mean values (SEM) of end tidal carbon dioxide tension ($P_{E'}CO_2$) at 1.5%, 1.0% and 0.5% halothane before (filled circles) and during carbon dioxide breathing (open circles). $^{***}p < 0.001$ for differences between measurements before and during carbon dioxide breathing. $^{☆☆}p < 0.01$, $^{☆☆☆}p < 0.001$ for differences between 1.5% and 1.0% as well as between 1.0% and 0.5% halothane.

Ventilation before and during carbon dioxide stimulation

For carbon-dioxide-free breathing tidal volume increased by 20% from 3.83 ml/kg (SEM 0.22) to 4.58 ml/kg (SEM 0.28) ($p < 0.001$) when halothane was decreased from 1.5% to 1.0%. Tidal volume was further enhanced by 35% to 6.18 ml/kg (SEM 0.37) ($p < 0.001$) when the end tidal halothane concentration was lowered to 0.5% (Fig. 2). At halothane 1.5% and 1.0% minute volume was, however, similar since the respiratory rate was decreased at 1% compared with at 1.5% ($p < 0.05$; Fig. 2). In spite of a further decrease in respiratory rate at 0.5% halothane, the greater tidal volume resulted in a higher minute volume compared with 1.0% halothane ($p < 0.001$; Fig. 2). End tidal carbon dioxide tension was virtually unchanged at 1.5% and 1.0% halothane since minute volume was the same, while the greater minute volume at 0.5% halothane reduced $P_{E'}CO_2$ ($p < 0.001$; Fig. 3).

During carbon dioxide stimulation tidal and minute volumes were greater than before carbon dioxide breathing at all three halothane concentrations but respiratory rate was unaffected by carbon dioxide (Fig. 2). At halothane 1.5%, minute volume increased by 16% during carbon dioxide breathing compared with before carbon dioxide stimulation while at 1.0%, the increase in minute ventilation was 36% and at 0.5%, 67% greater than control (Fig. 2). These differences in tidal and minute volumes at the three halothane concentrations were also accompanied by differences in end tidal carbon dioxide tensions (Fig. 3).

$P_{E'}CO_2$ changed rapidly at the start of carbon dioxide stimulation and more than 50% of the maximal change was reached within 10 seconds of carbon dioxide inhalation (Fig. 4). A continued increase in $P_{E'}CO_2$ was observed with 1.5% halothane during the 5 minutes of carbon dioxide stimulation. However, more than 80% of the total change in $P_{E'}CO_2$ at 1.0% and 0.5% halothane, was reached after 10–30 seconds (Fig. 4). Changes in tidal volume lagged behind

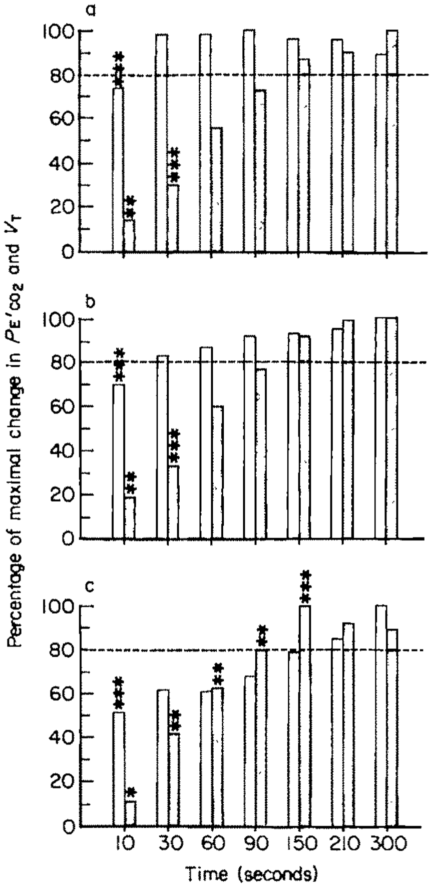


Fig. 4. Percentage of the maximal change in $P_{E'CO_2}$ (open columns) and V_T (filled columns) during, compared with just before carbon dioxide breathing, related to time (seconds). (a) Halothane 0.5%; (b) halothane 1.0%; (c) halothane 1.5%. Broken lines indicate 80% of maximal change. $^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.01$.

those of $P_{E'CO_2}$ at all three halothane concentrations and 80% of the total change of tidal volume during carbon dioxide stimulation was not reached until after 150 seconds (Fig. 4).

Respiratory drive and timing

For carbon-dioxide-free breathing maximum negative airway pressure during occlusion was less negative at 1.5% than at 1.0% ($p < 0.05$) or at 0.5% ($p < 0.001$) halothane (Fig. 5). Mean inspiratory flow was 5.4 ml/kg/second (SEM 0.3) at 1.5% halothane and increased significantly to 6.0 ml/kg/second (SEM 0.4) at 1.0% halothane ($p < 0.05$) and further to 7.0 ml/kg/second (SEM 0.5) at 0.5% halothane ($p < 0.01$). Inspiratory time was somewhat longer during 1.0% and was increased at 0.5% ($p < 0.01$) compared with during 1.5% halothane (Table 1), which also was the case for the inspiratory time of the occluded breath. The ratios of inspiratory time to duration of the whole breath for nonoccluded and occluded breaths were, however, unchanged by the halothane concentrations used (Table 1).

The occlusion pressure curves were biphasic with an initial fast phase and a later slow phase. The slopes ($\Delta P^o/\Delta t^o$) between these two phases were different at all three halothane concentrations (Table 2).

During carbon dioxide stimulation maximum negative airway pressure during occlusion was less negative with 1.5% than with 1.0% or 0.5% halothane ($p < 0.001$; Fig. 5). At all three halothane concentrations the value was, however, more pronounced compared with during carbon-dioxide-free breathing (Table 2). Mean V_T/T_I was 6.5 ml/kg/second (SEM 0.4) at 1.5% and increased to 8.1 ml/kg/second (SEM 0.5) at 1.0% ($p < 0.001$) and further to 11.6 ml/kg/second (SEM 0.8) at 0.5% halothane ($p < 0.001$). These were all higher than the corresponding V_T/V_I during carbon-dioxide-free breathing. For unoccluded breathing respiratory timing was uninfluenced by carbon dioxide at 1.5%, 1.0% and 0.5% halothane (Table 1).

During airway occlusions, however, inspiratory time was longer during carbon dioxide stimulation at 1.0% ($p < 0.01$) as well as at 0.5% ($p < 0.05$) halothane. This resulted in higher inspiratory time : total time of breaths ratios at 1.0% ($p < 0.05$) and 0.5% ($p < 0.01$) halothane during than before carbon dioxide stimulation (Table 1).

During occlusions, the slope of the fast phase was steeper for carbon dioxide stimulation than for carbon-dioxide-free breathing at all three halothane concentrations ($p < 0.05$; Fig. 5, Table 2). The slope of the initial phase was steeper than the slope of the later phase both with and without carbon dioxide stimulation. The slope of the slow phase was not influenced by carbon dioxide (Table 2).

Movements of ribcage and abdomen

Characteristic movements of the ribcage and abdomen in the three children studied are illus-

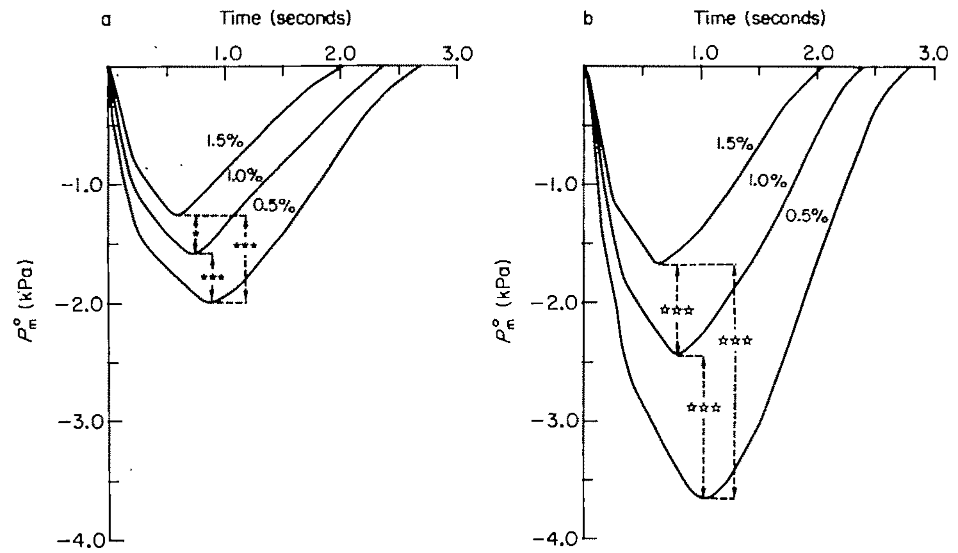


Fig. 5. Schematic presentation of mean values of airway occlusion pressure (P^o_m) versus time at 1.5%, 1.0% and 0.5% halothane (a) before and (b) during carbon dioxide breathing. ☆$p < 0.05$, ☆☆☆$p < 0.001$.

Table 1. Mean (SEM) values of durations of inspiration (T_I and T^o_I), T_I/T_{tot} and T^o_I/T^o_{tot} ratios before and during 4% carbon dioxide breathing at unoccluded and occluded breathing with 1.5%, 1% and 0.5% halothane.

	Halothane 1.5%		Halothane 1.0%		Halothane 0.5%	
	No CO_2	4% CO_2	No CO_2	4% CO_2	No CO_2	4% CO_2
Unoccluded						
T_I, seconds	0.73 (0.05)	0.73 (0.06)	0.78 (0.04)	0.78 (0.04)	0.89☆☆ (0.05)	0.88☆☆ (0.04)
T_I/T_{tot}	0.37 (0.02)	0.35 (0.02)	0.34☆ (0.02)	0.34 (0.02)	0.33 (0.02)	0.34 (0.02)
Occluded						
T^o_I, seconds	0.59 (0.05)	0.63 (0.06)	0.72☆☆** (0.05)	0.79☆☆☆ (0.06)	0.86☆☆* (0.07)	1.05☆☆ (0.09)
T^o_I/T^o_{tot}	0.31 (0.02)	0.31 (0.02)	0.31* (0.02)	0.35☆ (0.03)	0.34** (0.03)	0.39 (0.03)

☆$p < 0.05$, ☆☆$p < 0.01$, ☆☆☆$p < 0.001$ for differences between 1.5% and 1.0% and between 1.0% and 0.5% halothane.

*$p < 0.05$, **$p < 0.01$ for differences between carbon-dioxide-free breathing and breathing during 4% carbon dioxide inhalation.

trated in Fig. 6. At 1.5% halothane, the ribcage and abdomen moved in opposite directions. The ribcage retracted during most of inspiration both with and without carbon dioxide stimulation. At 1% halothane, movements during the early inspiratory phase were also paradoxical while expansion of the ribcage was found later during inspiration (Fig. 6). Ribcage movement was somewhat improved during carbon dioxide breathing at this halothane concentration. The observed paradoxical movement during inspiration was no longer present at 0.5% halothane. The expansion of the ribcage at this level of anaesthesia was much greater during carbon dioxide stimulation than at the other two halothane concentrations. The amplitude of abdominal movement was similar at all three halothane concentrations before as well as during carbon dioxide breathing, while ribcage participation in the ventilatory carbon dioxide response was improved at lower halothane concentrations (Fig. 6).

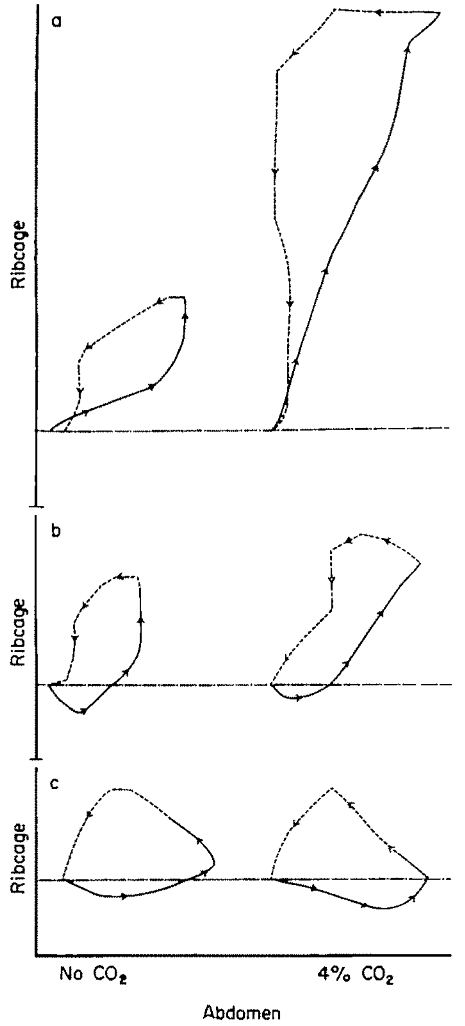


Fig. 6. Movement of ribcage and abdomen at 1.5%, 1.0% and 0.5% halothane before and during carbon dioxide breathing. (a) Halothane 0.5%; (b) halothane 1.0%; (c) halothane 1.5%. The interrupted horizontal line represents the pre-inspiratory resting position of ribcage and abdomen. The continuous portion of the curve indicates inspiration and the broken line, expiration.

Discussion

It was shown recently by Gallagher and Black[10] that for children of a similar age as ours, the ratio between end tidal and inspired halothane concentration was stable after 30 minutes. This is in agreement with the time needed in the present study before a stable end tidal halothane concentration was reached and, hence, no measurements were done until at least 30 minutes after induction. This time interval was also allowed when halothane concentrations were decreased to obtain end tidal concentrations of 1.0% and 0.5%. It is important that surgical stimuli are eliminated in order to study the influence of various concentrations of halothane on ventilation and regulation of breathing during anaesthesia. In this investigation children scheduled for hypospadias repair were selected and a caudal block was employed. The 30 minutes needed for gas equilibration were also considered to be long enough to establish the block before the start of surgery. Since the caudal block was performed after induction of anaesthesia, its evaluation could not be performed prior to surgery. Arterial blood pressure, heart rate and respiratory frequency were, however, carefully followed and in no case were there any changes in these variables due to the start of surgery.

Spontaneous breathing at a halothane concentration of 1.5% was characterised by smaller tidal volumes and higher respiratory rates than at the two lower concentrations, which suggests that the response to deeper halothane anaesthesia is based to some extent on adjustments of respiratory timing. Consequently, respiratory rhythm responses are not totally eliminated by halothane, as suggested previously by Duffin and Hung.[11] They found, in an animal experiment, that deepening the level of halothane anaesthesia failed to terminate and shorten inspiration and to cycle the respiratory act into expiration. In this study the duration of inspiration and of the whole respiratory cycle was, however, shorter at deeper anaesthetic levels. Duffin and Hung also suggested that the function of the respiratory motor centre was unaltered at various levels of halothane anaesthesia. Contrary to this, the mean inspiratory flow in the present study, was lower at a deeper anaesthetic level. This indicates a weakened inspiratory drive[12,13] which is also supported by the less negative occlusion pressures at 1.5% than at 1.0% and 0.5% halothane (Fig. 5). Since airway occlusion pressure reflects the neuronal output of the intended breath from the respiratory centre,[14] the present findings indicate a decreased phrenic nerve discharge to the diaphragm. Thus, deeper anaesthetic levels result in higher respiratory rates which demonstrate an active response from centres involved in respiratory timing, while dose dependent depression of respiratory motor functions was revealed.

Table 2. Mean (SEM) values of maximal intra-airway occlusion pressure (P°_{m}), the slope of the initial fast phase ($\Delta P^{\circ}/\Delta t^{\circ}$ (fast)) and of the following slow phase ($\Delta P^{\circ}/\Delta t^{\circ}$ (slow)) at 1.5%, 1.0% and 0.5% halothane before and during 4% carbon dioxide breathing.

	Halothane 1.5%		Halothane 1.0%		Halothane 0.5%	
	No CO_2	4% CO_2	No CO_2	4% CO_2	No CO_2	4% CO_2
P°_{m},	−1.28***	−1.68	−1.60☆***	2.44☆☆☆	2.03☆☆☆***	3.66☆☆☆
kPa	(0.1)	(0.17)	(0.19)	(0.26)	(0.22)	(0.39)
$\Delta P^{\circ}/\Delta t^{\circ}$ (fast),	3.6*	4.6	4.3*	5.2☆	4.6*	7.1
kPa/second	(0.45)	(0.5)	(0.56)	(0.4)	(0.6)	(1.5)
$\Delta P^{\circ}/\Delta t^{\circ}$ (slow),	1.7†	2.1††	2.0☆†††	2.4†††	2.0†††	3.3†††
kPa/second	(0.5)	(0.6)	(0.6)	(0.6)	(0.5)	(1.7)

☆ $p < 0.05$, ☆☆☆ $p < 0.001$ for differences between 1.5% and 1.0% and between 1.0% and 0.5% halothane.
* $p < 0.05$, *** $p < 0.001$ for differences between carbon-dioxide-free and 4% carbon dioxide breathing.
† $p < 0.05$, †† $p < 0.01$, ††† $p < 0.001$ for differences between fast and slow slopes ($\Delta P^{\circ}/\Delta t^{\circ}$).

At 4% carbon dioxide stimulation, a more depressed respiratory drive at 1.5% than at 1.0% and 0.5% halothane was confirmed while respiratory rate and timing were unchanged by the presence of carbon dioxide during inspiration. Thus, the normal carbon dioxide reactivity of centres involved in rhythm function in the awake state,[15–17] which results in increased rates, was depressed by halothane. While respiratory drive during carbon dioxide stimulation improved at more superficial levels of halothane anaesthesia, this was not the case with respiratory timing. In other words, the depression of respiratory rhythm function for carbon dioxide did not vary with the depth of halothane anaesthesia.

Regulation of breathing is a complex interaction between receptors, controllers and effectors, and the mechanisms behind ventilatory reactions to various levels of halothane, as well as to carbon dioxide provocation, are unknown. It can, however, be stated that respiratory drive and rate in this study depended on the level of anaesthesia while the ventilatory carbon dioxide response was dictated by variations in respiratory drive only. When changes of end tidal carbon dioxide tension and tidal volume were followed after the start of carbon dioxide breathing, a time difference between changes of carbon dioxide and V_T was shown. $P\mathrm{E}'\mathrm{CO}_2$ increased rapidly and after 10 seconds reached almost 80% of the total $P\mathrm{E}'\mathrm{CO}_2$ change at halothane concentrations of 1% and 0.5% (Fig. 4). At 1.5% it took longer, however, to reach 80% of the total change in $P\mathrm{E}'\mathrm{CO}_2$ and a stable level of $P\mathrm{E}'\mathrm{CO}_2$ was not reached during the 5 minutes of carbon dioxide breathing. On the other hand, at any of the halothane concentrations used, tidal volumes did not reach a stable level until at least 150 seconds elapsed after the start of carbon dioxide inhalation. This time lag between stable levels of change of $P\mathrm{E}'\mathrm{CO}_2$ and of tidal volume, shows that no immediate reflex response from carbon dioxide receptors was responsible. It rather seemed to depend either upon peripheral, slowly adapting carbon dioxide receptors[18] or on a time-dependent equilibration of carbon dioxide tensions between brain tissue and blood in the respiratory motor centre.

The respiratory depression due to halothane was characterised by smaller ventilation volumes, increased $P\mathrm{E}'\mathrm{CO}_2$, weakened respiratory drive and a less pronounced ventilatory carbon dioxide response at higher halothane concentrations. Investigations of ribcage and abdominal movements revealed that abdominal motions were less influenced by halothane concentrations than were those of the ribcage. This was shown earlier by Tusiewicz *et al.*[9] in children anaesthetised with halothane concentrations of 0.8–0.9%. Ribcage movements in the present series were, however, found to be highly dependent on halothane concentrations. At 1.5% halothane, breathing was clearly paradoxical with inward movements of the ribcage. This was less pronounced at 1.0% and eliminated at an end tidal halothane concentration of 0.5% (Fig. 6). The mechanism behind this could be neurogenic or muscular. Since the ribcage motions were influenced by carbon dioxide at a halothane concentration of 0.5%, a neurogenic cause seems more likely because a 4% carbon dioxide stimulation *per se* is not expected to enhance the contractility of skeletal muscles. This paradoxical chest wall movement found at 1.5% halothane is of great importance not only as an indicator of inefficient ventilation in clinical practice but also for the study of lung mechanics using oesophageal pressures. Paradoxical breathing will result in false oesophageal pressures[19] which, therefore, do not accurately reflect intrapleural pressures. This makes calculations of dynamic compliance and total pulmonary resistance inappropriate.

It is concluded that respiration was severely depressed at an end tidal halothane concentration of 1.5% and in the absence of surgical stimuli. This resulted in small tidal volumes and high end tidal carbon dioxide concentrations which to some extent were compensated by increased respiratory rates. The ventilatory carbon dioxide response improved at more superficial anaesthetic levels while respiratory timing was unresponsive to carbon dioxide irrespective of the halothane concentration used. At 1.5% halothane, breathing was paradoxical with the ribcage moving inwards. However, ribcage movements improved and paradoxical breathing disappeared at more superficial levels of anaesthesia.

Acknowledgments

This study was supported by grants from the Medical Faculty, University of Lund, Sweden and from the Swedish Medical Research Council, Stockholm (Project No. B 86-19X-07189-02A).

References

1. Fourcade HE, Stevens WC, Larson CP, Cromwell TH, Bahlman SH, Hickey RF, Halsey MJ, Eger EI II. The ventilatory effects of Forane, a new inhaled anesthetic. *Anesthesiology* 1971; **35:** 26–31.
2. Marsh HM, Rehder K, Hyatt RE. Respiratory timing and depth of breathing in dogs anaesthetized with halothane or enflurane. *Journal of Applied Physiology* 1981; **51:** 19–25.
3. Munson ES, Larson CP Jr, Babad AA, Regan MJ, Beuchel DR, Eger EI II. The effects of halothane, fluroxene and cyclopropane on ventilation: a comparative study in man. *Anesthesiology* 1966; **27:** 716–28.
4. Eger EI II, Dolan WM, Stevens WC, Miller RD, Way WL. Surgical stimulation antagonizes the respiratory depression produced by Forane. *Anesthesiology* 1972; **36:** 544–9.
5. Calverley RK, Smith NT, Jones CW, Prys-Roberts C, Eger EI II. Ventilatory and cardiovascular effects of enflurane anesthesia during spontaneous ventilation in man. *Anesthesia and Analgesia* 1978; **57:** 610–8.
6. Murat I, Delleur MM, Macgee K, Saint-Maurice C. Changes in ventilatory patterns during halothane anesthesia in children. *British Journal of Anaesthesia* 1985; **57:** 569–72.
7. Knill RL, Gelb AW. Ventilatory responses to hypoxia and hypercapnia during halothane sedation and anesthesia in man. *Anesthesiology* 1978; **49:** 244–51.
8. Lindahl SGE, Olsson A-K. Respiratory drive and timing before and during CO_2 inhalation in infants anesthetized with halothane. *European Journal of Anaesthesiology* 1986; **3:** 427–37.
9. Tusiewicz K, Bryan AC, Froese AB. Contributions of changing rib cage–diaphragm interactions to the ventilatory depression of halothane anesthesia. *Anesthesiology* 1977; **47:** 327–37.
10. Gallagher TM, Black GW. Uptake of volatile anaesthetics in children. *Anaesthesia* 1985; **40:** 1073–7.
11. Duffin J, Hung S. Respiratory rhythm generation. *Canadian Anaesthetists' Society Journal* 1985; **32:** 124–37.
12. Jordan C. Assessment of the effects of drugs on respiration. *British Journal of Anaesthesia* 1982; **54:** 763–82.
13. Germain M, Wahba WM, Gillies DMM. Ventilation following induction of general anaesthesia with thiopentone. *Canadian Anaesthetists' Society Journal* 1982; **29:** 100–4.
14. Milic-Emili J, Whitelaw WA, Derenne JP. New tests to assess lung function: occlusion pressure—a simple measure of the respiratory center's output. *New England Journal of Medicine* 1975; **293:** 1029–30.
15. Avery ME, Chernick V, Dutton RE, Permutt S. Ventilatory response to inspired carbon dioxide in infants and adults. *Journal of Applied Physiology* 1963; **18:** 895–903.
16. Remmers JE. Analysis of ventilatory response. *Chest* 1976; **70** (Suppl.): 134–7.
17. Lindroth M. Mechanical ventilation in newborn infants. Pulmonary mechanics and follow-up studies. Thesis, University of Lund, Lund, Sweden, 1980.
18. Coleridge HM, Coleridge JCG, Banzett RB. Effect of CO_2 on afferent vagal endings in the canine lung. *Respiration Physiology* 1978; **34:** 135–51.
19. LeSouëf PN, Lopes JM, England SJ, Bryan MH, Bryan AC. Influence of chest wall distortion on esophageal pressure. *Journal of Applied Physiology* 1983; **55:** 353–8.

Anaesthesia, 1987, Volume 42, pages 1276–1283

Comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation

Studies following valvular heart surgery

K. M. SHERRY, J. P. W. WINDSOR AND R. O. FENECK

Summary

The cardiorespiratory effects of intermittent positive pressure ventilation and high frequency jet ventilation with and without positive end expiratory pressure were compared in patients following valvular heart surgery (mitral and/or aortic). Twenty patients received intermittent positive pressure ventilation and high frequency jet ventilation with 0, 0.5 and 1.0 kPa positive end expiratory pressure. High frequency jet ventilation was well tolerated. The addition of 1.0 kPa positive end expiratory pressure was associated with preservation of the arterial oxygen tension without any increase in shunt or significant adverse haemodynamic effect. The results are discussed and compared with a previous study of high frequency jet ventilation following aortocoronary bypass graft surgery.

Key words

Ventilation; intermittent positive pressure breathing, high frequency jet, positive end expiratory pressure.

In 1967, Sanders[1] introduced the technique of ventilation of the lungs using high pressure gas driven through a small cannula with consequent air entrainment by the Venturi principle. Four years later, Jonzon *et al.*[2] introduced the concept of high frequency positive pressure ventilation (HFPPV) using tidal volumes just above conventionally measured deadspace values, with respiratory rates of 60–100 breaths/minute. The delivery of high frequency ventilation using the jet injector principle (HFJV) was introduced by Klain and Smith in 1977.[3]

It has been suggested that high frequency ventilation (HFV) has a number of advantages over conventional intermittent positive pressure ventilation (IPPV), including lower mean intrapulmonary pressures and, consequently, minimal effects on cardiac output,[4] improvement of various haemodynamic indices[3,5,6] and less disturbance of endocrine function.[2] In addition, the achievement of adequate alveolar ventilation with lower mean intrapulmonary pressure[5,7] and lower peak airway pressure[7–9] is likely to result in less pulmonary barotrauma.[8–11]

A previous study[12] reported the effects of HFV in patients following cardiac surgery and we have investigated patients following elective aortocoronary bypass graft surgery (ACBG).[13] However, patients with mitral and/or aortic valve disease differ from patients with ischaemic heart disease in a number of respects, including the volume and distribution of pulmonary blood flow, lung compliance and diffusion capacity.[14] Consequently, we elected to study patients with

---

K.M. Sherry, FFARCS, J.P.W. Windsor, FFARCS, Senior Registrars, R.O. Feneck, FFARCS, Consultant, Department of Anaesthesia, The London Chest Hospital, Bonner Road, London E2.

Correspondence should be addressed to Dr R.O. Feneck please.

0003–2409/87/121276 + 08 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

valvular heart disease as a separate group and compare the effects of IPPV with those of HFJV on cardiorespiratory function at different peak, mean and end expiratory airway pressures (P_{aw}).

Methods

Twenty adult patients (12 male) who presented for mitral (12) or aortic (8) valve surgery were studied after they had given written consent. Anaesthetic premedication consisted of oral diazepam and intramuscular papaveretum with hyoscine. Anaesthesia was induced using a benzodiazepine, opioid, myoneural relaxant sequence and the trachea intubated with a tracheal tube designed to facilitate HFJV (Mallinckrodt Hi-Lo jet tube). The left radial artery was cannulated and a triple lumen flow-directed pulmonary artery cather introduced via the right internal jugular vein. Radial artery, pulmonary artery and right atrial pressure waveforms were displayed. Body temperature, urine output and lead II of the electrocardiograph were monitored throughout the operation. After surgery, patients were transferred to the intensive care unit where conventional IPPV was continued.

Each study started after the clinical condition of the patient had been stable for one hour, that is, there had been no change in respiratory or haemodynamic status and no change in vasodilator, inotropic, fluid or blood requirements. No patient required any alteration in therapy during the study period. Patients were assigned randomly to one of two groups, designating the sequence in which IPPV and HFJV with and without positive end expiratory pressure (PEEP) were to be applied (Table 1).

Table 1. Sequence in which IPPV and HFJV with and without PEEP were applied to patients in groups 1 and 2.

Group 1	IPPV1	$HFJV_0$	$HFJV_{0.5}$	$HFJV_{1.0}$	IPPV2
Group 2	IPPV1	$HFJV_{1.0}$	$HFJV_{0.5}$	$HFJV_0$	IPPV2

IPPV was delivered using a Brompton Manley ventilator with a tidal volume (V_T) of 10 ml/kg, an inspiratory to expiratory ratio (I:E) of 1:2.5 and a fractional inspired oxygen concentration ($F\text{IO}_2$) of 1.0. Minute volume was adjusted to maintain the arterial carbon dioxide tension ($P\text{aCO}_2$) between 4.5 and 5.0 kPa.

HFJV was delivered using an Acutronic MK800 ventilator (Acutronic AG). The system is shown in Fig. 1 and has been described previously.[13] The oxygen–air blender was set to deliver an $F\text{IO}_2$ of 1.0 and PEEP was applied to the expiratory limb of the T-piece by a water manometer. The ventilator was set to deliver 150 breaths/minute with an inspiratory time of 30% of the respiratory cycle. The driving gas pressure and, hence, the minute ventilation was adjusted to maintain $P\text{aCO}_2$ between 4.5 and 5.0 kPa. In order to ensure cardiorespiratory stability, at least 30 minutes were allowed to elapse following alterations in ventilation or the level of PEEP before a series of readings was taken. Haemodynamic and airway pressures, body temperature, heart rate and cardiac out-

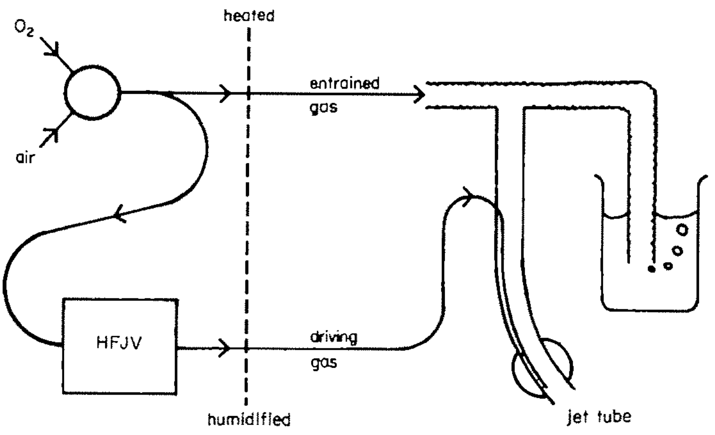


Fig. 1. Ventilator system used to deliver HFJV with PEEP.

put ($\dot{Q}_t$) were measured and recorded, and arterial blood samples analysed as described previously.[13] Shunt fraction ($\dot{Q}_s/\dot{Q}_t$) and total tissue oxygen delivery (flux) were calculated using standard formulae.

Statistical analysis was performed using one-way analysis of variance, and paired or unpaired t-tests as appropriate.

Results

The demographic data are shown in Table 2; the groups were comparable in all respects. There were no significant differences between the groups in respect of inotropic or vasodilator therapies.

Table 2. Patient data presented as mean (SEM).

	Group 1 (n = 10)		Group 2 (n = 10)	
Age, years	60.3	(2.7)	62.7	(3.8)
Weight, kg	71.3	(3.8)	65.9	(3.1)
Surface area, sq.m	1.82	(0.07)	1.71	(0.04)
Blood loss, ml/hour	26.5	(7.3)	35.7	(6.2)
Urine output, ml/hour	77.7	(10.4)	82.5	(17.9)

The effects of changing from IPPV to HFJV

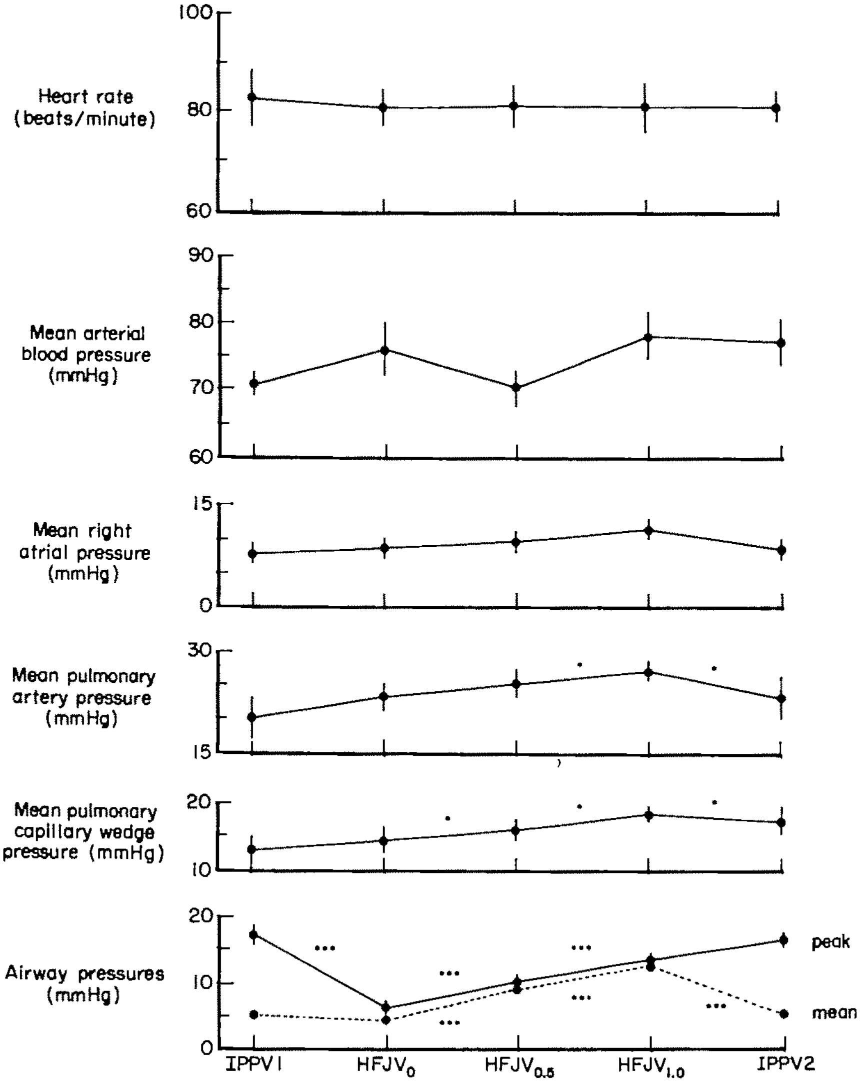


Fig. 2. Plots of heart rate (HR), systemic blood pressure (BP), right atrial pressure (RAP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) and peak and mean airway pressures (P_{aw}) during IPPV and HFJV with increasing PEEP. * $p < 0.05$; *** $p < 0.001$.

with increasing PEEP and back to IPPV in group 1 are shown in Figs 2 and 3. The effects of changing from IPPV to HFJV with decreasing PEEP are shown in Figs 4 and 5. In each figure, the effects on peak and mean P_{aw} that resulted from change of the mode of ventilation and the application of additional PEEP are shown.

Group 1

There was a significant decrease in peak P_{aw} and Pa_{O_2}, no change in mean P_{aw} and an increase in $\dot{Q}_s/\dot{Q}_t$ on changing from IPPV to HFJV. As PEEP was increased to 1.0 kPa there were increases in peak P_{aw}, mean P_{aw}, pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP). Finally, on transfer from $HFJV_{1.0}$ to IPPV there were significant decreases in mean P_{aw}, PAP and PCWP but $\dot{Q}_t$ and flux increased.

Group 2

Transfer from IPPV to $HFJV_{1.0}$ was associated

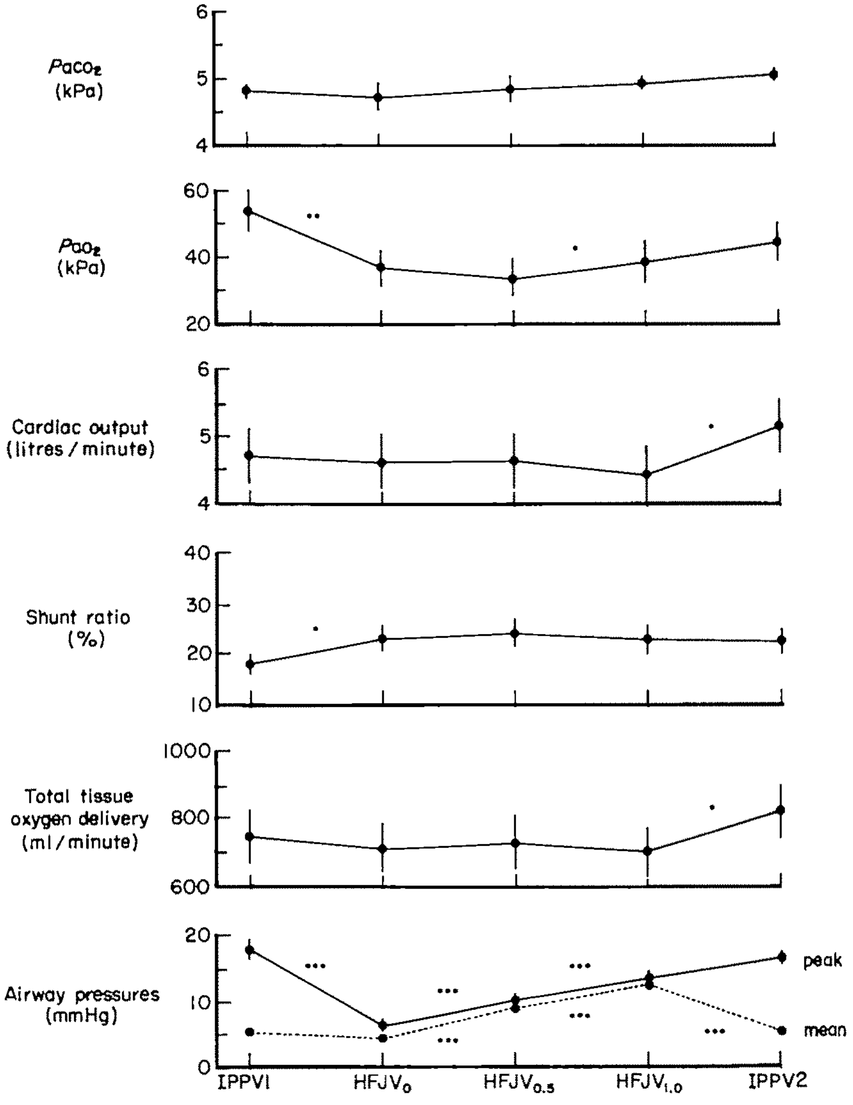


Fig. 3. Plots of Pa_{CO_2}, Pa_{O_2}, cardiac output ($\dot{Q}_t$), shunt ratio ($\dot{Q}_s/\dot{Q}_t$), tissue oxygen delivery (flux) and peak and mean airway pressures (P_{aw}) during IPPV and HFJV with increasing PEEP. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

with increases in mean P_{aw}, right atrial pressure (RAP), PAP and PCWP. Pa_{O_2}, $\dot{Q}_t$ and flux remained unchanged. As PEEP was decreased, peak P_{aw}, mean P_{aw}, RAP, PAP and PCWP were reduced but there were no significant changes in any other parameter. On final transfer from HFJV$_0$ to IPPV there was an increase in peak P_{aw}.

Discussion

All patients who participated in this study were drawn from the same population and had a comparable and uncomplicated postoperative course. Furthermore, the Pa_{CO_2} values were comparable in each group and reflect stable and effective ventilation throughout the study.

The HFJV settings used during this study were derived from our clinical experience with the technique. There is evidence that respiratory rates greater than 150 breaths/minute may have adverse haemodynamic effects[15] and that longer inspiratory times may cause alveolar overdistension,[15,16] an increase in mean P_{aw} and a reduction in $\dot{Q}_t$.[17–19] At a respiratory rate of

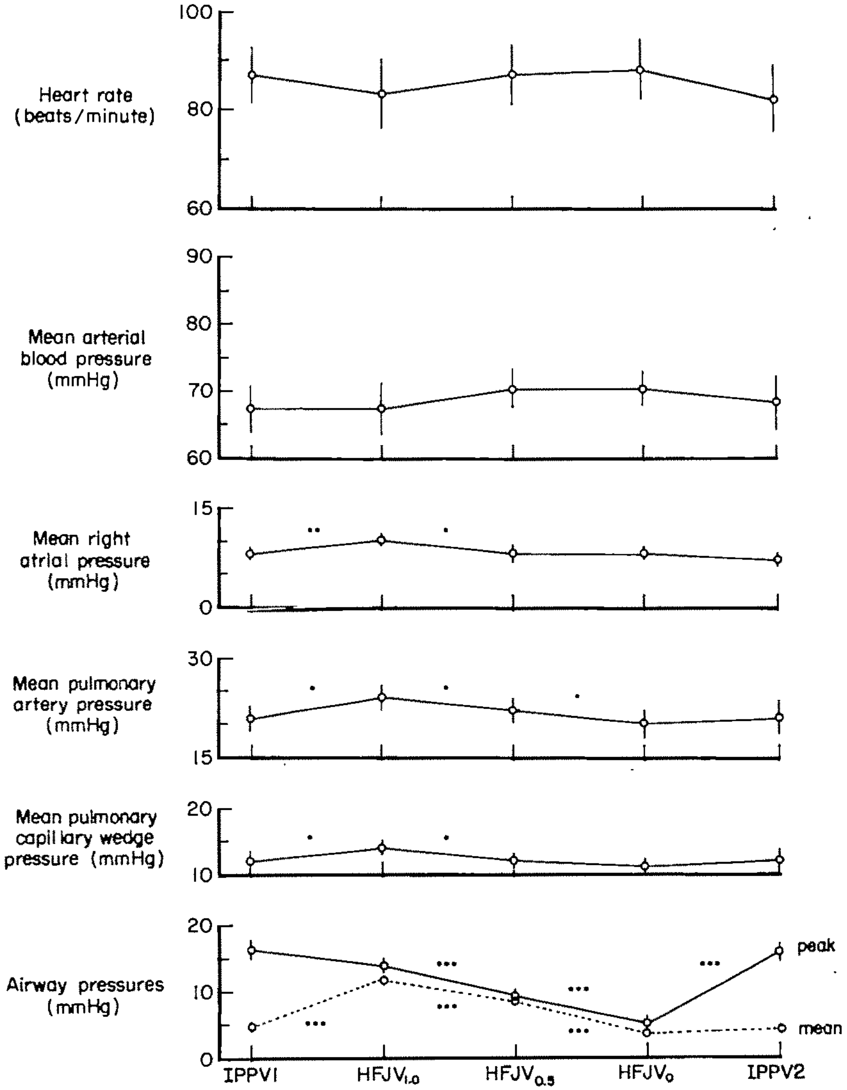


Fig. 4. Plots of heart rate (HR), systemic blood pressure (BP), right atrial pressure (RAP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) and peak and mean airway pressures (P_{aw}) during IPPV and HFJV with decreasing PEEP. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

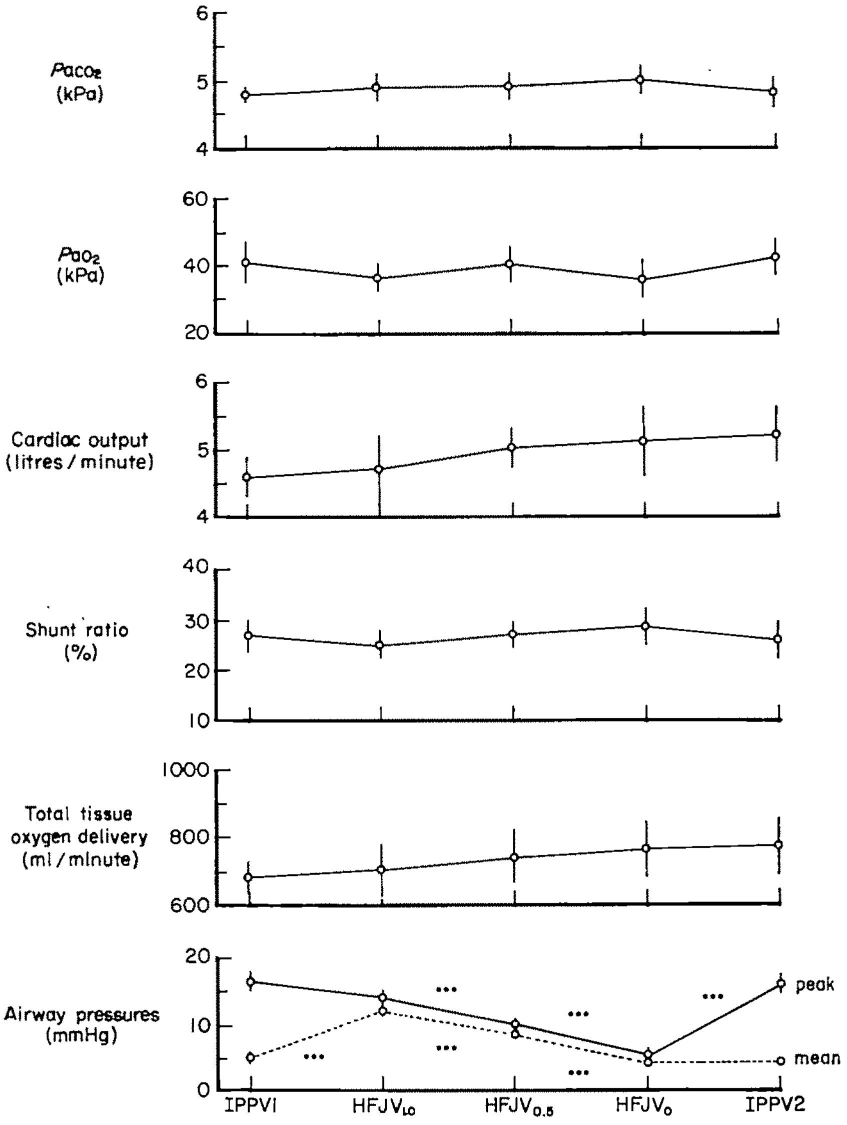


Fig. 5. Plots of $Pa\text{CO}_2$, $Pa\text{O}_2$, cardiac output ($\dot{Q}_t$), shunt ratio ($\dot{Q}_s/\dot{Q}_t$) tissue oxygen delivery (flux) and peak and mean airway pressures (P_{aw}) during IPPV and HFJV with decreasing PEEP. *** $p < 0.001$.

150 breaths/minute with an inspiratory time of 30% of the ventilation cycle, a minor degree of PEEP is inherent in the system since the time constant of the lung and chest wall is exceeded by the expiratory time.[3,16] In this study, the inherent PEEP in the system was 0.1–0.3 kPa. Further levels of PEEP were added using a water manometer; thus the levels of PEEP at $\text{HFJV}_{0.5}$ and $\text{HFJV}_{1.0}$ were relative values.

There is often a progressive clinical improvement in the circulation in the first few hours following cardiopulmonary bypass surgery. The cardiac index improved by 3 hours in a previous study of HFJV following cardiac surgery; the authors conceded that this was likely to be due in part to recovery from anaesthesia and surgery and not solely to the pattern of ventilation.[12] In order to determine whether changes seen during this study resulted from the pattern of ventilation rather than an improvement in the circulation during the study period, we compared the following parameters during IPPV both before and after HFJV: heart rate (HR), systemic arterial pressure, RAP, PAP, PCWP, $\dot{Q}_t$, arterial blood gas tensions, peak P_{aw}, mean P_{aw}, $\dot{Q}_s/\dot{Q}_t$ and flux. On paired comparisons there were no significant differences in group 2; however, when the second period of IPPV was compared with the first in group 1 there was a decrease in $P\text{ao}_2$ and an increase in $\dot{Q}_s/\dot{Q}_t$ without any change in the haemodynamic data or in flux. This was felt to reflect a persistence of the changes seen in this group following the start of HFJV. These comparisons suggest that the circulation was stable and that any haemodynamic changes seen during HFJV were likely to be the consequences of the pattern of ventilation at different peak, mean and end expiratory P_{aw}.

During HFJV without additional PEEP, there was a decrease in peak P_{aw} in comparison to IPPV. The addition of PEEP to the high frequency circuit increased peak P_{aw} and mean P_{aw} to values equal to or greater than those seen during IPPV. Indeed, mean P_{aw} during $\text{HFJV}_{1.0}$ almost doubled in comparison to the control value.

Comparisons within the two groups of patients in this study showed uniform increases in RAP, PAP and PCWP in association with increases in mean P_{aw} and PEEP; these changes reflect the increase in intrathoracic pressure. There were no significant haemodynamic changes on changing directly from IPPV to HFJV_0 in group 1 or from HFJV_0 to IPPV in group 2. There was no haemodynamic impairment on changing from IPPV to $\text{HFJV}_{1.0}$ in group 2; however, the change from $\text{HFJV}_{1.0}$ to IPPV in group 1 resulted in a significant increase in both $\dot{Q}_t$ and flux. It is difficult to explain these differences; however, patients with left-sided valvular heart disease often have a reduced pulmonary compliance and high pulmonary artery pressure and, in the early post-bypass period, may have a rigidity of the pulmonary circulation which protects against transmission of increased airway pressure to the circulation. Overall lung stiffness may be reduced in the later recovery period as the crystalloid load acquired during cardiopulmonary bypass is cleared by the kidneys, and the effects of changing airway and intrathoracic pressures may then be reflected in the systemic haemodynamics.

A decrease in $P\text{ao}_2$ is a common observation following transfer from IPPV and HFJV and some authors have advocated the use of a higher $F\text{io}_2$ with the addition of PEEP to counteract this trend.[10,20] We found an acute decrease in $P\text{ao}_2$ following transfer from IPPV to HFJV_0 in group 1, associated with an increase in $\dot{Q}_s/\dot{Q}_t$ but no change in $\dot{Q}_t$. The transfer from IPPV to $\text{HFJV}_{1.0}$ in group 2 patients was associated with a large increase in mean P_{aw} but no changes in $P\text{ao}_2$, $\dot{Q}_s/\dot{Q}_t$ or $\dot{Q}_t$. Thus the application of extra PEEP to HFJV in the early post-bypass period appeared to prevent the decrease in $P\text{ao}_2$ commonly seen on transfer to HFJV.

The benefit of HFJV with PEEP in the early post-bypass period following valvular heart surgery is in direct contrast to our findings in patients following ACBG. It is therefore of interest to compare these two studies. Peak P_{aw} and mean P_{aw} were similar. Initial RAP, PAP and PCWP were higher in patients following valve surgery but the increases with added PEEP were comparable. However, the two studies differed in two important respects: patients in the valve study were able to tolerate large increases in mean P_{aw} without significant haemodynamic impairment, and the increase in mean P_{aw} prevented the decrease in $P\text{ao}_2$ and increase in $\dot{Q}_s/\dot{Q}_t$. Both of these findings differ from our observations in patients following ACBG.

Patients with left heart valvular disease tend to develop chronic pulmonary venous congestion, which results in a high pulmonary artery pressure, pulmonary arteriolar hypertrophy, especially in the lower lobes, and diversion of blood to the upper zones of the lungs. These pathological changes lead to altered lung mechanics: specifically, decreased lung compliance, decreased diffusion capacity and ventilation/perfusion ratio inequalities.[14] In addition, these patients often have a reduced cardiac output and a high left atrial pressure so that on exertion, pulmonary oedema is readily precipitated and lung mechanics deteriorate further. In contrast, patients with coronary artery disease uncomplicated by cardiac failure usually have normal pre-operative lung function. The difference in findings between our two studies may be attributable to protection conferred by the rigid, hypertrophied walls of the pulmonary vessels in patients with valve disease against the effects of intrathoracic pressure changes on the circulation. One implication is that the recommended limit of a respiratory rate of 150 breaths/minute and an inspiratory time of 30% in order to prevent adverse haemodynamic effects, may be applicable to patients with essentially normal lungs but some patients may tolerate, or indeed benefit from, the increased mean airway pressures associated with higher respiratory rates and a longer inspiratory time. However, this remains speculative and, at present, there is insufficient information on the cardiorespiratory effects of HFJV in patients following valvular surgery for us to refute the established recommendations.

In conclusion, we have shown that high frequency ventilation is well tolerated by patients during recovery from valvular heart surgery. The addition of 0.5 and 1.0 kPa PEEP to HFJV appears to protect against intrapulmonary shunting in this group of patients, without adverse haemodynamic effects.

Acknowledgments

The authors thank Mr R.K. Walesby, Consultant Cardiothoracic Surgeon, for permission to study patients under his care, and Sister C. Kwok and the nursing staff of the Intensive Care Unit at the London Chest Hospital for their help. This work was supported by a grant from the Clinical Research Committee, The National Heart and Chest Hospitals, London.

References

1. SANDERS RD. Two ventilating attachments for bronchoscopes. *Delaware Medical Journal* 1967; **37**: 170–5.
2. JONZON A, OBERG PA, SEDIN G, SJOSTRAND U. High-frequency positive-pressure ventilation by endotracheal insufflation. *Acta Anaesthesologica Belgica* 1971; **43** (Suppl.): 1–43.
3. KLAIN M, SMITH RB. High frequency percutaneous transtracheal jet ventilation. *Critical Care Medicine* 1977; **5**: 280–7.
4. SJOSTRAND U. High-frequency positive-pressure ventilation (HFPPV): a review. *Critical Care Medicine* 1980; **8**: 345–64.
5. DAVEY AJ, LEIGH JM. High frequency venturi jet ventilation. Adult respiratory distress syndrome—a case report. *Anaesthesia* 1982; **37**: 670–4.
6. ERIKSSON I, JONZON A, SEDIN G, SJOSTRAND U. The influence of the ventilatory pattern on ventilation, circulation and oxygen transport during continuous positive-pressure ventilation. An experimental study. *Acta Anaesthesiologica Scandinavica* 1977; **64** (Suppl.): 149–63.
7. WILLATTS SM. Alternative modes of ventilation. II. High and low frequency positive pressure ventilation, PEEP, CPAP inversed ratio ventilation. *Intensive Care Medicine* 1985; **11**: 115–22.
8. CARLON GC, KAHN RC, HOWLAND WS, RAY C JR, TURNBULL AD. Clinical experience with high frequency jet ventilation. *Critical Care Medicine* 1981; **9**: 1–6.
9. CARLON GC, RAY C JR, KLAIN M, MCCORMACK PM. High-frequency positive-pressure ventilation in management of a patient with bronchopleural fistula. *Anesthesiology* 1980; **52**: 160–2.
10. CARLON GC, HOWLAND WS, RAY C JR, MIODOWNIK S, GRIFFIN JP, GROEGER JS. High-frequency jet ventilation. A prospective randomized evaluation. *Chest* 1983; **84**: 551–9.
11. GEORGE RJD, GEDDES DM. High frequency ventilation. *British Journal of Hospital Medicine* 1985; **33**: 344–9.
12. SHINOZAKI T, DEANE RS, PERKINS FM, COFFIN LH, ITTLEMAN FP, MAZUZAN JE, BIRD FM. Comparison of high-frequency lung ventilation with conventional mechanical lung ventilation. Prospective trial in patients who have undergone cardiac operations. *Journal of Thoracic and Cardiovascular Surgery* 1986; **89**: 269–74.
13. NORMANDALE J, PATRICK M, SHERRY KM, FENECK RO. Comparison of conventional intermittent positive pressure ventilation with high frequency jet ventilation. Studies following aortocoronary bypass graft surgery. *Anaesthesia* 1987; **42**: 824–34.
14. HARRIS P, HEATH D. *The human pulmonary circulation*, 2nd edn. New York: Churchill Livingstone, 1977.
15. GIOIA FR, ROGERS MC. High frequency ventilation of the lungs. In: ATKINSON RS, ADAMS AP, eds. *Recent advances in anaesthesia and analgesia, Vol. 15.* Edinburgh: Churchill Livingstone, 1985: 63–78.
16. SYKES MK. High frequency ventilation. *Thorax* 1985: **40**: 161–5.
17. CHAKRABARTI MK, SYKES MK. Cardiorespiratory effects of high frequency intermittent positive pressure ventilation in the dog. *British Journal of Anaesthesia* 1980; **52**: 475–82.
18. GALLAGHER TJ, KLAIN M, CARLON GC. Present status of high frequency ventilation. *Critical Care Medicine* 1982; **10**: 613–7.
19. JIMENEZ LENDINEZ M, CAMBRONERO JA, LOPEZ J, GALVIN B, GARCIA A, DENIA R, AGUADO A. Airway pressure as a determining factor for ventilation and haemodynamic efficiency during HFJV. In: SCHECK PA, SJOSTRAND U, SMITH RB, eds. *Perspectives in high frequency ventilation.* Boston: Martinus Nijhoff, 1985: 81–6.
20. SLADEN A, GUNTUPALLI K, KLAIN M, ROMANO R. High frequency jet ventilation and conventional ventilation: a comparison of cardiorespiratory parameters. In: SCHECK PA, SJOSTRAND U, SMITH RB, eds. *Perspectives in high frequency ventilation.* Boston: Martinus Nijhoff, 1985: 251–61.

Anaesthesia, 1987, Volume 42, pages 1284–1286

CASE REPORT

Liver tumours and muscle relaxants

Electromyographic studies in children

T. C. K. BROWN, M. GREGORY, B. BELL AND P. C. CAMPBELL

Summary

Electromyographic studies of the onset of action of tubocurarine or alcuronium were performed on eight occasions in five patients who had liver masses. There was a slow onset of action and an increased dose requirement in those with malignant disease. Normal responses were found in a patient with benign nodular hyperplasia and in another where the malignant tumour was successfully treated with chemotherapy.

Key words

Co-existing disease; malignant disease.
Complications; muscle relaxant resistance.

Liver tumours are uncommon in children and occur in two or three patients per year in our hospital. We have had a total of 50 patients; 29 had liver lobectomies and in 22 of these the tumour was malignant. The clinical observation that patients with tumours sometimes have a slow onset of paralysis and require larger doses than usual, led us to monitor our patients with electromyography. This paper presents eight studies on five children who presented with liver masses.

Methods

The median nerve was stimulated at the wrist and the electrical activity of opponens pollicis recorded and integrated using the integrated electromyograph designed and built at Monash University, Melbourne.[1] The patients, aged 2, 3, 4 and 12 years, were induced with thiopentone followed by either tubocurarine 0.66 mg/kg or alcuronium 0.3 mg/kg and the onset of paralysis monitored. Additional doses of relaxant were given when relaxation was inadequate prior to tracheal intubation.

Results

Table 1 summarises the patient information and the pathological findings. The integrated electromyographs (IEMG) of four studies using tubocurarine are presented in Fig. 1. In two patients the onset of relaxation was so slow that 3 minutes after injection muscle activity had decreased by less than 15%, so additional doses of 0.33 and 0.66 mg/kg were given (A and B in Fig. 1). In the third patient the IEMG had decreased only to 32% activity after 9 minutes and an additional 0.33 mg/kg was given (C2). These patients had malignant hepatoblastoma, hepatic sarcoma and rhabdomyosarcoma. The fourth patient, who had a large irregular mass which turned out to be benign nodular hyperplasia, had a normal re-

---

T.C.K. Brown, MD, FFARACS, Director of Anaesthesia, M. Gregory, MB, ChB, FFARCS, Research Fellow, B. Bell, BAppSci, Research Assistant, P.C. Campbell, MB, BS, MCPA, FRCPA, Director of Anatomical Pathology, Royal Children's Hospital, Parkville, Victoria 3052, Australia.

0003–2409/87/121284 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

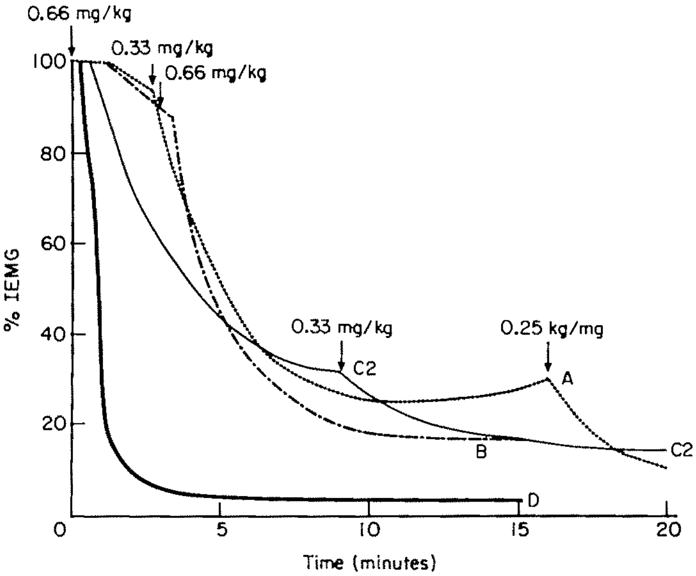


Fig. 1. IEMG responses to tubocurarine in three patients with liver tumours who showed a slow onset of paralysis and the need for additional doses. The fourth patient (D) had a normal IEMG response and was found to have benign liver disease.

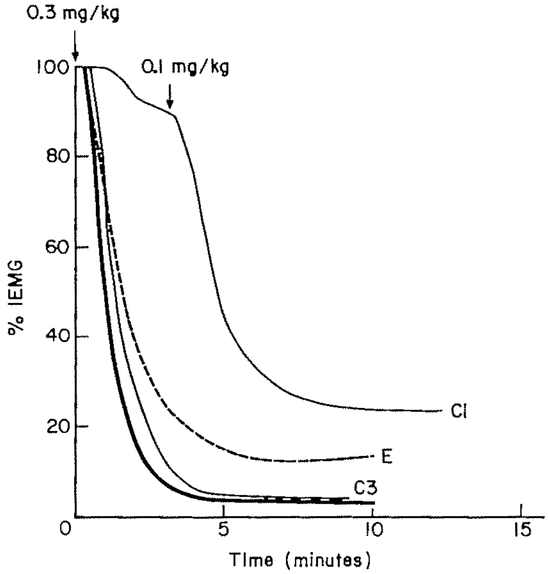


Fig. 2. IEMG responses to alcuronium in two patients with malignant tumours (C and E). Normal response (mean for 65 patients) shown by heavy line. Patient E had two identical responses. C3 was after successful chemotherapy in patient C.

Table 1. Patients' ages and pathological details.

Patient	Age (years)	Size	Site	Necrotic areas	Diagnosis
A	4	11 × 10 × 10 cm	Left lobe	Yes	Embryonal sarcoma
B	4	10 cm diameter	Right lobe	No	Epithelial hepatoblastoma
C2	2	Biopsy		No	Embryonal sarcoma
C3	2	8 cm diameter	Right lobe	No	No viable tumour
D	12	Multiple nodules	Left lobe	No	Focal nodular hyperplasia
E	3	10 × 8 × 8 cm	Right lobe	Yes	Mixed hepatoblastoma

sponse to tubocurarine (D) when compared with 34 normal patients.

Figure 2 shows the results of four studies following alcuronium 0.3 mg/kg administered to two patients with malignant tumours. Two studies done a few days apart in one child who had a hepatoblastoma showed identical responses (E in Fig. 2). The other patient showed marked resistance and required an additional dose of 0.1 mg/kg alcuronium to produce adequate anaesthetic conditions for angiography (C1). A few days later he showed resistance to tubocurarine (above) when an open biopsy was performed (C2 in Fig. 1). Following chemotherapy the response in this child changed towards the pattern seen in normal patients (C3 in Fig. 2).

Discussion

The response to non-depolarising relaxants is altered in children with malignant liver tumours so that the onset of paralysis is slow and increased doses are required. One patient with a benign mass and another successfully treated with chemotherapy had normal responses. The child who had two studies done a few days apart showed that the response is consistent in a given patient.

The reason for the altered responses is not yet known. The presence of binding sites in the tumour which often have a generous blood supply in an organ which receives 20–25% of cardiac output, is the possible mechanism for removal of relaxant before its distribution to muscle. Another factor might be altered protein binding but, so far, there is inadequate evidence for either of these theories.

The reversion to a normal response after chemotherapy, when the tumour was no longer viable, suggests the possibility that the response to muscle relaxants may be useful in assessing the success of chemotherapy. An altered response to relaxants has been observed with other tumours in children and will be the subject of another paper.

Reference

1. Lam HS, Ng KC, Cass NM. Electromyographic monitoring of neuromuscular block. *British Journal of Anaesthesia* 1981; **53:** 1351–7.

Anaesthesia, 1987, Volume 42, pages 1287–1290

CASE REPORT

Severe acute asthma and the menstrual cycle

R. J. LENOIR

Summary

Three cases of severe acute asthma associated with menstruation are reported. All required admission to an intensive therapy unit and intermittent positive pressure ventilation of the lungs for one week or more. Several bronchodilator drugs and anaesthetic agents were employed in an effort to reduce the severe bronchospasm. In each case, improvement appeared to coincide with the end of menstruation. An awareness of the association of asthma and menstruation by those involved in intensive therapy may help in the management of similar cases.

Key words

Complications; asthma.

It is not generally realised by those involved in intensive therapy that severe exacerbations of acute asthma can be caused by hormonal changes in the menstrual cycle. Not infrequently, young female patients are admitted to the intensive therapy unit (ITU) with severe asthma resistant to conventional therapy. To date, no hormonal therapy has been shown to be therapeutic in this situation. However, the use of a variety of therapies, each with inherent potential complications, might be reduced if premenstrual or menstrual asthma (PMA) were more widely recognised.

The case histories of three patients are presented to illustrate the problem.

Case histories

Case 1

A 41-year-old Nigerian woman was admitted to the emergency department with severe acute asthma. She was a known labile asthmatic with a past history of frequent admissions. Rapid deterioration occurred and the arterial carbon dioxide tension ($Pa\text{CO}_2$) increased from 6 to 10 kPa; tracheal intubation and mechanical ventilation were instituted. Airway pressures were high despite treatment with steroids, aminophylline and salbutamol, and the administration of large doses of sedatives and pancuronium. Some improvement occurred after 24 hours and spontaneous ventilation was resumed; however, her condition deteriorated soon afterwards and mechanical ventilation was re-instituted.

Airway pressure remained high during the next week despite administration of numerous sedatives and muscle relaxants, ether, ketamine and Althesin in attempts to improve the bronchospasm. The bronchospasm did improve soon after an Althesin infusion was started one week

---

R.J. Lenoir, MB, BCh, FFARCS, Senior Registrar, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

Present address: Department of Anaesthesia, Princess Mary's Royal Air Force Hospital, Halton, Aylesbury, Bucks HP22 5PS.

0003–2409/87/121287 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

after admission but this also coincided with the end of one week of menstruation.

The patient developed other complications during the course of her illness, such as infection, negative potassium and nitrogen balance and peripheral muscle weakness. Consequently, full weaning from ventilatory support did not take place until 23 days after admission. On subsequent questioning, the patient admitted that she had noted previous deterioration of her asthma in relation to menstrual periods.

Case 2

A 22-year-old Indian woman presented with dyspnoea and wheeze. She gave a history of asthma since childhood and had been treated intermittently with courses of steroids since 4 years of age. She had experienced two previous severe attacks, one of which required admission to ITU. Her current therapy comprised salbutamol and beclomethasone inhalers. On admission she was able to talk but improved only slightly after treatment with nebulised ipratropium and salbutamol, and intravenous aminophylline and hydrocortisone. She was admitted to ITU for observation. There was a sudden deterioration at 02:30 hours on the third day after admission and $P\text{aCO}_2$ increased to 6.2 kPa. A salbutamol infusion was started in case the nebulised therapy did not reach the distal airways but since this produced no improvement, the patient's trachea was intubated and the lungs were ventilated mechanically. Airway pressures varied between 4.5 and 7 kPa; a supraventricular tachycardia of 165 beats/minute was treated inappropriately with practolol, which caused an increase in airway pressure to 7.5 kPa. Halothane delivered from a Boyle's machine through a Servo 900C ventilator reduced the bronchospasm; airway pressure decreased to 3.7 kPa initially and subsequently settled at about 5–6 kPa. The patient was menstruating from the fifth to the ninth day, after which a dramatic improvement of bronchospasm occurred. She was rapidly weaned and her trachea was extubated although later she became fatigued and her $P\text{aCO}_2$ increased to 7 kPa; artificial ventilation was required for another 2 days.

On later questioning, a previous history of increased anxiety and wheezing prior to menstruation was elicited.

Case 3

A 31-year-old woman, a known asthmatic since childhood, was admitted with severe wheezing, dyspnoea and cyanosis. Her condition deteriorated despite standard therapy with hydrocortisone, aminophylline and nebulised salbutamol, and she required artificial ventilation. Airway pressures in excess of 6 kPa were recorded and both ether inhalation and a ketamine infusion were tried without success. Positive end expiratory pressure (PEEP) 0.5 kPa was used at one stage to increase closing volume and to reduce air trapping;[1] later, massive surgical emphysema developed and periods of spontaneous respiration were allowed but were limited by an increasing $P\text{aCO}_2$. Menstruation started 3 days after admission and it was not until 7 days after admission that any improvement of bronchospasm was noted. The patient was discharged from ITU 10 days after admission.

Discussion

Menstrual exacerbations of asthma have been recognised for many years[2,3] and there is evidence that asthma is more common in females after puberty than before.[4,5] A study by Hanley[6] showed that one-third of women with asthma have a significantly reduced peak expiratory flow rate (PEFR) during the premenstrual and menstrual period. These women also have more severe asthma and are more likely to be admitted to hospital than other women with asthma. Progesterone has been shown to stimulate ventilation[7] and cause a mid-cycle decrease in $P\text{aCO}_2$[8] but there is little data on the effects of hormone therapy on menstrual asthma. Gibbs *et al.*[9] showed that 40% of women who attended as outpatients for asthma reported premenstrual deterioration but no correlation was found between this deterioration and premenstrual tension, consumption of aspirin, use of the contraceptive pill or behaviour of asthma during pregnancy. In their discussion, the authors put forward evidence[10–14] to support the theory that PMA is caused by a reduction in progesterone levels but noted that no controlled clinical trial had been undertaken.

A more recent study stimulated by the observation of three cases of severe menstrual exacerbation of asthma,[15] confirmed the association in 33% of 57 patients. The exacerbations were maximal in the premenstrual phase and 13 (68%)

of the patients so affected had been hospitalised, compared with only 10 (26%) of those whose asthma was not affected by menstruation. Premenstrual and menstrual symptoms correlated significantly with pulmonary symptom scores in the PMA group and twice as many of these patients required steroids compared to those with regular asthma.

There is evidence that prostaglandin F2α levels may be involved in the mechanism of PMA[16–18] but the results of two clinical studies have suggested that severity of PMA is not related to the use of antiprostaglandin analgesics taken for dysmenorrhoea.[9,15] Another explanation for premenstrual exacerbations of asthma is an alteration in immune mechanisms.[19]

Sudden death from asthma can occur during the premenstrual period. Two sisters died after they were admitted at the same phase of the menstrual cycle just after puberty.[20]

In view of the association between asthma and menstruation, clinicians should consider PMA in women of childbearing age admitted to ITU with severe asthma. The three cases described here illustrate that despite strenuous efforts to control and improve the severe bronchospasm, it may be resistant to conventional therapy until the end of the menstrual period.

In the first case, sudden improvement occurred one week after admission, soon after an Althesin infusion was started. This led to speculation that reactive bronchospasm, precipitated by the presence of the tracheal tube, might have been a problem and that this was abolished by anaesthesia with Althesin. However, ether inhalation was used for 30 minutes on the fourth day after admission with no effect. An alternative explanation for her improvement on the seventh day is that the hormonal stimulus to asthma did not abate until menstruation ceased.

The second patient showed a typical premenstrual exacerbation of asthma; she was admitted to hospital 4 days before her period started. Two days later, there was a sudden deterioration in the early hours of the morning. It is possible that diurnal rhythm[21] as well as menstrual rhythm may have contributed to the deterioration.

The third patient also developed severe asthma resistant to conventional therapy in relation to her period and her condition improved only when menstruation stopped; therapy was unchanged at the time.

Other causes of exacerbation of asthma, such as infection and allergy, must of course be excluded and standard management includes adequate sedation while on a ventilator, physiotherapy and mobilisation of mucus plugs, bronchodilators and steroids, as in any case of severe acute asthma. If airway pressures do not decrease in spite of these measures, the clinician may feel somewhat reassured in patients with PMA that symptoms are likely to resolve when menstruation ceases. Because of the possibility that premenstrual exacerbations of asthma may be caused by reduced endogenous progesterone levels,[9] controlled clinical trials of progesterone therapy in asthma with premenstrual association appear to be warranted. It is possible that such therapy may reduce the frequency and severity of asthma in this situation.

Acknowledgments

I am grateful to Dr D. R. G. Browne, Consultant Anaesthetist in charge of ITU and Dr S. W. Clarke, Consultant Physician at the Royal Free Hospital, and to Dr M. A. Stern, Consultant Immunologist at Leicester General Hospital and Dr R. J. White, Consultant Physician at Southmead Hospital, Bristol for permission to publish details of patients under their care.

References

1. Qvist J, Andersen JB, Pemberton M, Bennike KA. High-level PEEP in severe asthma. *New England Journal of Medicine* 1982; **307**: 1347–8.
2. Claude F, Allemany R. Asthma and menstruation. *Presse Medicale* 1938; **46**: 755–9.
3. Urbach E, Gottlieb PM. *Allergy*. New York: Grune and Stratton, 1946: 571.
4. Dawson B, Horobin G, Illsley R, Mitchell R. A survey of childhood asthma in Aberdeen. *Lancet* 1969; **1**: 827–30.
5. Schachter J, Higgins MW. Median age at onset of asthma and allergic rhinitis in Tucumseh, Michigan. *Journal of Allergy and Clinical Immunology* 1976; **57**: 342–51.
6. Hanley SP. Asthma variation with menstruation. *British Journal of Diseases of the Chest* 1981; **75**: 306–8.
7. Goodland RL, Reynolds JG, McCoord AB, Pommerenke WT. Respiratory and endocrine effects induced by estrogen and progesterone. *Fertility and Sterility* 1953; **4**: 300–17.
8. England SJ, Farhi LE. Fluctuations in alveolar CO_2 and in base excess during the menstrual cycle. *Respiratory Physiology* 1976; **26**: 157–61.

9. Gibbs CJ, Coutts II, Lock R, Finnegan OC, White RJ. Premenstrual exacerbation of asthma. *Thorax* 1984; **39:** 833–6.
10. Frank RT. The hormonal causes of premenstrual tension. *Archives of Neurology and Psychiatry* 1931; **26:** 1053–7.
11. Beaumont GE. Ovarian asthma. In: *The clinical approach to medical practice*. London: J. & A. Churchill, 1956: 57–61.
12. Brush MC. Endocrine and other biochemical factors in the aetiology of the premenstrual syndrome. *Current Medical Research and Opinion* 1979; **6** (Suppl. 5): 19.
13. Dalton K. Menstruation and accidents. *British Medical Journal* 1960; **2:** 1425–6.
14. Briggs MH, Brotherton J. *Steroid biochemistry and pharmacology*. London: Academic Press, 1970.
15. Eliasson O, Scherzer HH, De Graff AC. Morbidity in asthma in relation to the menstrual cycle. *Journal of Allergy and Clinical Immunology* 1986; **77:** 87–94.
16. Parker CW, Snider DE. Prostaglandins and asthma. *Annals of Internal Medicine* 1973; **78:** 963–5.
17. Eliasson O, Longo M, Dore-Duffy P, Densmore MJ, De Graff AC. Prostaglandin F2α in serum and pulmonary response to sodium meclofenamate and metaproterenol in relation to the menstrual cycle in asthmatic women. *American Review of Respiratory Disease* 1985; **131:** A41.
18. Koullapis EN, Collins WP. The concentration of 13,14-dihydro-15-oxo-prostaglandin F2α in peripheral venous plasma throughout the normal ovarian and menstrual cycle. *Acta Endocrinologica* 1980; **93:** 123–8.
19. Ozkaragoz K, Cakin F. The effects of menstruation on immediate skin reactions in patients with respiratory allergy. *Journal of Asthma Research* 1970; **7:** 171–5.
20. Barkman RP. Sudden death in asthma. *Medical Journal of Australia* 1981; **1:** 316–7.
21. Barnes P, Fitzgerald G, Brown M, Dollery C. Nocturnal asthma and changes in circulating epinephrine, histamine, and cortisol. *New England Journal of Medicine* 1980; **303:** 263–7.

Anaesthesia, 1987, Volume 42, pages 1291–1293

CASE REPORT

Lupus anticoagulant

Implications for obstetric anaesthetists

A. M. MALINOW, W. J. K. RICKFORD, B. L. K. MOKRISKI, D. N. SALLER AND W. J. McGUINN

Summary

Circulating lupus anticoagulant occurs in 5–37% of all patients with systemic lupus erythematosus. Its occurrence is not restricted to collagen vascular disease states. Lupus anticoagulant causes a prolongation of certain laboratory coagulation studies yet it is associated in vivo with a history of systemic intravascular thromboses. Placental vessels are also affected. Less than one in six pregnancies complicated by the presence of this auto-antibody is successful. Treatment of afflicted parturients with anti-platelet therapy has increased perinatal survival rates. Derangements in the coagulation profile and concomitant anti-platelet therapy confound the rational use of regional anaesthesia in the management of labour and delivery in these high-risk pregnancies.

Key words

Blood; coagulation, anticoagulant.
Complications; systemic lupus erythematosus.

Lupus anticoagulant is an auto-antibody which inhibits *in vitro* coagulation tests. This immunoglobulin (usually IgG, sometimes IgM), first described in patients with systemic lupus erythematosus,[1] occurs in 5–37% of patients with the condition.[2] About one-half of patients with lupus anticoagulant do not have systemic lupus erythematosus or similar disease states. Lupus anticoagulant has also been found in a variety of other conditions that include connective tissue diseases, lymphoma, carcinoma and myeloproliferative diseases.[1] Lupus anticoagulant complicates pregnancy. Its presence is associated with a high degree of fetal wastage and maternal vascular thrombosis.[1,3,4] The disease is more highly associated with thrombosis than with bleeding but the laboratory tests used to profile the disorder and various drugs used in the treatment of this disease may complicate the choice of obstetric anaesthesia for the afflicted parturient.

Case history

A 27-year-old gravida 2, para 0, abortus 1 with a diagnosis of systemic lupus erythematosus (SLE) and known lupus anticoagulant, presented to the labour and delivery suite at 38 weeks' gestation for induction of labour. She had a 6-year history of diagnosed systemic lupus erythematosus highlighted by episodes of polyarthralgia and arthritis. She miscarried in 1980

A.M. Malinow, MD, Assistant Professor, W.J.K. Rickford, FFARCS, FFARCSI, Visiting Assistant Professor, B.L.K. Mokriski, MD, Instructor in Anesthesiology, D.N. Saller, Jr, MD, Instructor in Obstetrics and Gynecology, W.J. McGuinn, MD, Fellow in Obstetric Anesthesiology, Departments of Anesthesiology, Obstetrics and Gynecology, University of Maryland Medical System, 22 S. Greene Street, Baltimore, Maryland 21201, USA.

0003–2409/87/121291 + 03 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

at 20 weeks' gestation, with an obstetric diagnosis of a cord accident. She had acute left lower extremity arterial insufficiency 4 years previously. A coagulation profile done before emergency arteriography then gave first evidence of the presence of a circulating lupus anticoagulant. A femoropopliteal artery bypass under general anaesthesia was performed. During the present pregnancy, she presented to the University Hospital High Risk Obstetric Service at 16 weeks' gestation. A coagulation profile revealed a prothrombin time of 12.7 seconds (normal 11–12.6 seconds) and an activated partial thromboplastin time of 54 seconds (normal 27–36 seconds). She was started on aspirin 80 mg/day; the last dose was taken the morning of admission into the labour and delivery suite.

Results of an amniocentesis one day previously were compatible with fetal lung maturity. Her cervix was judged favourable for induction on pelvic examination. Her haematocrit was 33.7%, platelet count 154 000/ml, bleeding time 4.2 minutes (normal 1–7 minutes), prothrombin time 11.3 seconds and activated partial thromboplastin time 48 seconds. Labour was induced and an oxytocin infusion commenced but she was not in spontaneous, active labour at the end of the first day of induction. The oxytocin infusion was discontinued and re-started the next morning. Her cervix was 4 cm dilated but the fetal head was floating at the end of the second day. It was decided to perform a Caesarean section; epidural analgesia was not requested.

After oral treatment with 30 ml Bicitra (sodium citrate 500 mg/5 ml and citric acid 334 mg/5 ml) and preloading of the circulation with Hartmann's solution, general anaesthesia was induced with thiopentone 300 mg and suxamethonium 100 mg and the trachea intubated. Cricoid pressure was employed during induction and left uterine displacement employed until delivery. Anaesthesia was maintained with 50% nitrous oxide in oxygen and 0.5% halothane. A male child was delivered, with Apgar scores of 8 at both 1 and 5 minutes. The halothane was then discontinued, morphine 10 mg given intravenously and the nitrous oxide concentration increased to 70%. Muscle relaxation was maintained with a 0.1% infusion of suxamethonium. Estimated blood loss was 1500 ml. The 24-hour postpartum haematocrit was 23% and platelet count 73 000/ml.

The neonate was diagnosed later as having a tracheo-oesophageal fistula which was subsequently repaired surgically.

Discussion

This case presents an interesting problem for the obstetric anaesthetist, namely the choice of the appropriate anaesthetic technique. Lupus anticoagulant appears to interfere with platelet phospholipid coagulation by binding to antigenic determinant sites on the phospholipid portion of prothrombinase (formed by the interaction of factor X_a and factor V_a, and platelet phospholipid in the presence of calcium ions). Activated partial thromboplastin times and kaolin clotting times are often prolonged but the prothrombin time is prolonged only rarely.[1,2] The original cases of lupus anticoagulant were reported in patients with haemorrhagic diathesis but its presence is usually associated with thrombosis and not with bleeding.[1,2]

In a recent report, the incidence of thrombosis in a group of 219 patients with lupus anticoagulant was 28%. It did not matter whether or not the patients had SLE-like disease.[1] Both arterial and venous thromboses have been reported. Thromboses occur most commonly in the lower extremities but occasionally in the pulmonary, retinal or even intracranial vasculature.[1] Bleeding in these patients has been ascribed most often to a qualitative or quantitative deficiency in platelet function or number, to a deficiency in prothrombin or to an additional haemorrhagic diathesis such as von Willebrand's disease.[1,2] Bleeding due to the lupus anticoagulant alone is rare and it seems to be an *in vitro* phenomenon.

The presence of lupus anticoagulant in pregnancy is ominous. Reviews of the literature[3,4] reveal perinatal survival rates of only 10–15% and the second trimester fetal death rate is unusually high (up to about 30%).[4] Thromboembolic disease, chorea gravidarum, idiopathic thrombocytopenia purpura, false positive tests for syphilis (RPR), intra-uterine growth retardation and fetal death may occur. It appears that the thrombotic process that occurs systemically may affect the placenta as well. Infarction and necrosis have been described.[3,4] Of interest also is the fact that plasma containing lupus anticoagulant will inhibit the vascular production of prostacyclin, a potent vasodilator and platelet aggregation inhibitor.[5] Altered prostacyclin–

thromboxane ratios have been found in preeclamptic women.[6]

There have been recent reports of dramatic improvement in the perinatal survival rate with an antepartum regimen of low dose aspirin and steroids.[4,7] In one report,[4] these pharmacological measures along with earlier identification of these women, vigilant fetal surveillance and preterm delivery when appropriate, decreased the rate of pregnancy loss to 37.5%.

There is a dearth of information in the anaesthetic literature about the risks of conduction anaesthesia in patients with lupus anticoagulant. The anaesthetic implications of the laboratory manifestation of lupus anticoagulant and the concomitant aspirin treatment are obvious but confusing. These patients often have partial thromboplastin times prolonged past the upper acceptable limit for major conduction anaesthesia.[8] In our patient the value was 50% over control early in pregnancy and did not improve dramatically on aspirin therapy. In addition, the patient's bleeding time was normal. Yet recent reports now warn of the possible haemorrhagic diathesis of patients who receive aspirin[9,10] even with normal bleeding times.[11] On the other hand, patients with lupus anticoagulant tend to thrombose and not to bleed. There is one report of a small series of nonpregnant patients who presented for nerve blocks. These patients, although they received aspirin, had epidural anaesthesia without evidence of subsequent haematoma formation.[12] The benefits of epidural analgesia in a labouring woman may help reduce catecholamine-induced vasoconstriction to a placenta with already compromised perfusion.

This patient was seen before the oxytocin induction of labour began and after haematological studies had been performed. Physical examination did not reveal any anatomical abnormalities that would raise doubts about the ability to establish an airway. The option of conduction anaesthesia was offered for analgesia in labour. The fetal benefits of such analgesia, in our opinion, warranted taking the possible, yet improbable, risk of epidural bleeding and this was explained to the patient. She was informed that if conduction anaesthesia was not already established and abdominal delivery were obstetrically indicated, then general anaesthesia would be required. The anaesthesia team thought that the benefit of conduction anaesthesia to the well-being of the fetus for abdominal delivery was no better than for general anaesthesia. The maternal risk of epidural haematoma would then outweigh the possibility of failure to establish an airway.

References

1. Gastineau DA, Kazmier FJ, Nichols WL, Bowie EJW. Lupus anticoagulant: an analysis of the clinical and laboratory features of 219 cases. *American Journal of Hematology* 1985; **19:** 265–75.
2. Espinoza LR, Hartmann RC. Significance of the lupus anticoagulant. *American Journal of Hematology* 1986; **22:** 331–7.
3. Lubbe WF, Liggins GC. Lupus anticoagulant and pregnancy. *American Journal of Obstetrics and Gynecology* 1985; **153:** 322–7.
4. Branch DW, Scott JR, Kochenour NK, Hershgold E. Obstetric complications associated with lupus anticoagulant. *New England Journal of Medicine* 1985; **313:** 1322–6.
5. Walsh SW, Behr MJ, Allen NH. Placental prostacyclin production in normal and toxemic pregnancies. *American Journal of Obstetrics and Gynecology* 1985; **151:** 110–5.
6. Carreras LO, Defreyn G, Machin SJ, Vermylen J, Deman R, Spitz B, van Assche A. Arterial thrombosis, intrauterine death and "lupus" anticoagulant; detection of immunoglobulin interfering with prostacyclin formation. *Lancet* 1981; **1:** 244–6.
7. Lubbe WF, Palmer SJ, Butler WS, Liggins GC. Fetal survival after prednisone suppression of maternal lupus-anticoagulant. *Lancet* 1983; **1:** 1361–3.
8. Ostheimer GW. *Anesthetic management of obstetric emergencies. ASA Refresher Course 256.* ASA Annual Refresher Course Lectures. Park Ridge, IL: American Society of Anesthesiologists, Inc., 1986.
9. Mayumi T, Dohi S. Spinal subarachnoid hematoma after lumbar puncture in a patient receiving antiplatelet therapy. *Anesthesia and Analgesia* 1983; **62:** 777–9.
10. Greensite FS, Katz J. Spinal subdural hematoma associated with attempted epidural anesthesia and subsequent continuous spinal anesthesia. *Anesthesia and Analgesia* 1980; **59:** 72–3.
11. Hindman BJ, Koka BV. Usefulness of post-aspirin bleeding time. *Anesthesiology* 1986; **64:** 368–70.
12. Benzon HT, Bruner EA, Vaisrub N. Bleeding time and nerve blocks after aspirin. *Regional Anesthesia* 1983; **9:** 86–9.

Anaesthesia, 1987, Volume 42, pages 1294–1297

CASE REPORT

Prolonged bradycardia and hypotension after neostigmine administration in a patient receiving atenolol

J. ELDOR, B. HOFFMAN AND J. T. DAVIDSON

Summary

A 78-year-old woman admitted for an elective hip operation was maintained on atenolol for control of her hypertension. She received neostigmine and atropine for reversal of muscle relaxation at the end of general anaesthesia. She then developed prolonged bradycardia and hypotension which necessitated the use of adrenaline and isoprenaline. Such an adverse reaction with atenolol has not been described previously.

Key words

Complications; bradycardia, hypotension.
Drug interactions.

Maintenance of beta-adrenoreceptor blockade up to and including the day of surgery has been shown to reduce the occurrence of supraventricular tachydysrhythmias[1] with greater cardiovascular stability[2,3] in the peri-operative period. We present a case of prolonged bradycardia and hypotension after anaesthesia and reversal of residual neuromuscular blockade with neostigmine, in a patient taking atenolol. To our knowledge, this is the first reported case of such a reaction with atenolol.

Case history

A 78-year-old woman was admitted electively for a revision of a left total hip replacement due to a loose acetabular component. Her past history included a right mastectomy and chemotherapy for carcinoma of the breast, with no recurrence or metastases; she also had hypertensive ischaemic heart disease with stable angina pectoris which was treated with isosorbide dinitrate 80 mg/day, glyceryl trinitrate skin patch 5 mg/day and atenolol 50 mg/day.

On admission the patient weighed 65 kg, the arterial blood pressure was 150/90 mmHg, pulse rate 60 beats/minute and she was in sinus rhythm. Pre-operative serum potassium was 3.7 mmol/litre and urea, 5.8 mmol/litre. The ECG and chest X ray were within normal limits.

A pulse rate of 100 beats/minute and sinus rhythm were found at the pre-anaesthetic visit and her medication with atenolol was therefore, continued on the day of surgery. In addition, a 10 mg oral dose of diazepam was given for premedication.

The arterial blood pressure was 120/70 mmHg and the pulse rate 72 beats/minute before induction of anaesthesia. Anaesthesia was induced with droperidol 5 mg, fentanyl 100 μg, thiopentone 250 mg and suxamethonium 100 mg to facilitate tracheal intubation. A period of sinus bradycardia of 48–50 beats/minute with an arterial blood pressure of 80/50 mmHg followed

---

J. Eldor, MD, Senior Physician, B. Hoffman, MD, House Officer, J.T. Davidson, MD, FFARCS, Professor and Head of Department, Department of Anaesthesia, Hadassah Medical Center, Ein Karem, P.O. Box 12000, Jerusalem 91120, Israel.

0003–2409/87/121294 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

induction and responded to atropine 0.5 mg, ephedrine 2.5 mg and fluid loading. The arterial blood pressure and pulse rate soon returned to pre-induction levels. The central venous pressure (CVP) was 7 cm H_2O and a 12-lead ECG demonstrated no change in comparison to the pre-operative ECG.

Pancuronium bromide 6 mg was used for muscular relaxation and isoflurane 0.8–1.5% with 50% nitrous oxide in oxygen for maintenance of anaesthesia. Arterial blood pressure during most of the procedure was 120/80 mmHg and the pulse rate was 75 beats/minute with a CVP of 7–8 cm H_2O.

Twice during the operation sinus bradycardia of 45–50 beats/minute accompanied by an arterial blood pressure decrease to 80/50 mmHg was observed. The bradycardia and hypotension responded in both instances to atropine 0.5 mg, ephedrine 2.5 mg and a temporary decrease in inspired isoflurane concentrations. The CVP was stable at 7–8 cm H_2O. Isoflurane was discontinued 30 minutes before the end of surgery and pethidine 50 mg was administered over 10 minutes to provide postoperative analgesia. The operation lasted 4 hours and the estimated blood loss was 800 ml. Two units of packed blood cells, 3700 ml Ringer's lactate solution and 500 ml polygeline were administered intra-operatively.

The arterial blood pressure was 140/70 mmHg, pulse rate 70 beats/minute and the CVP 10 cm H_2O, so atropine 1 mg and neostigmine 2.5 mg were given to reverse the neuromuscular block. A sinus bradycardia of 30–35 beats/minute and a systolic blood pressure of 50 mmHg developed. An additional dose of atropine 1 mg and ephedrine sulphate 10 mg had no effect. An infusion of isoprenaline was commenced and after 200 μg had been administered the heart rate increased to 96 beats/minute, but the systolic blood pressure remained at 50 mmHg. The administration of calcium chloride 1 g had no haemodynamic effect. Therefore adrenaline 0.5 mg was administered intravenously and caused an immediate increase in arterial blood pressure and pulse rate. A short episode of ventricular tachycardia was treated successfully with lignocaine 75 mg intravenously and the pulse rate returned to 96 beats/minute. The arterial blood pressure continued to increase for one minute and peaked at 250/150 mmHg. ST depression was evident at that point on the ECG monitor. A nitroglycerine infusion (1 μg/kg/minute) was started which decreased the arterial blood pressure to 120/70 mmHg. The pulse rate decreased to 80 beats/minute with sinus rhythm and the ST depression disappeared. The patient awoke, began to breathe spontaneously and her trachea was extubated. A 12-lead ECG performed after extubation demonstrated no change from the pre-operative ECG.

The patient was transferred for further haemodynamic monitoring to the intensive care unit where she remained for 36 hours and was haemodynamically stable, with an arterial blood pressure of 110/60 mmHg and a pulse rate of 50 beats/minute. Cardiac enzymes demonstrated an increase in creatine phosphokinase the day after surgery, which returned to normal after 36 hours. Other enzymes were within normal limits. The patient was discharged from the orthopaedic department 2 weeks later.

Discussion

Profound bradycardia has been reported after the use of neostigmine, even when used with atropine, to reverse neuromuscular blockade in patients receiving beta-blockers.[4–7] Sprague[4] reported a decrease in the pulse rate from 60 to 30 beats/minute following intravenous administration of neostigmine 2.5 mg and atropine 1.25 mg to a patient receiving propranolol 40 mg every 12 hours for control of supraventricular tachycardia. Prys-Roberts[5] reported that pulse rate always decreased to less than 45 beats/minute following the administration of neostigmine to patients with renovascular hypertension which was treated with large doses (10–36 mg/kg) of propranolol. Wagner *et al.*,[6] however, failed to show any significant slowing of the pulse rate in dogs given atropine plus neostigmine or atropine plus pyridostigmine 10 minutes after beta-blockade was induced with an intravenous dose of 0.25 mg/kg propranolol. Seidl and Martin[7] reported a case of a 51-year-old woman, receiving nadolol for treatment of hypertension and angina, who developed prolonged and refractory bradycardia and hypotension after anaesthesia with thiopentone, fentanyl and pancuronium and reversal of neuromuscular blockade with neostigmine.

We have reported a case of prolonged bradycardia and hypotension when neostigmine and atropine were given for reversal of neuromuscular blockade at the conclusion of anaesthesia in a patient receiving oral atenolol. The muscarinic effects of neostigmine are due mainly to the accumulation of acetylcholine at muscarinic receptors on cholinergic effector sites. The muscarinic blocking drug atropine is used to antagonise competitively this action of acetylcholine. Owens *et al.*[8] found that the incidence of cardiac dysrhythmia following reversal of neuromuscular blocking agents in geriatric patients who received a halogenated anaesthetic, was five times greater after neostigmine than after pyridostigmine.

Atenolol is a beta$_1$-selective (cardioselective) adrenoreceptor blocking drug without partial agonist or membrane stabilising activity.[9] Its profile of action most closely resembles that of metoprolol, which differs only in that it has some membrane stabilising activity. Atenolol is effective in the treatment of hypertension and in the prophylactic management of angina pectoris. Its narrow dose response rate obviates the need for highly individualised dose titration. In patients with angina its long duration of beta-blocking activity allows once daily dosage, whereas other beta-blockers, unless in sustained release dosage forms, need to be given in divided doses. As with metoprolol, atenolol is preferable to nonselective beta-blockers in patients with asthma or diabetes mellitus.

The duration of effect of single oral doses of atenolol on exercise heart rate at 25 hours after ingestion, as compared with the maximum effect at 3 hours, was 37% with 25 and 50 mg, 69% with 100 mg and 84% with 200 mg.[10] Recent studies have shown that 86% of beta-adrenoreceptors in human left ventricle are beta$_1$ subtype; the balance of 14% are beta$_2$ adrenoreceptors.[11] This may account for the relative failure of atenolol and metoprolol (but not propranolol) to block an isoprenaline tachycardia, because isoprenaline stimulates both beta-adrenoreceptor subtypes.[12]

If it becomes necessary to increase the inotropic state of the myocardium, beta-adrenoreceptor agonists are effective but the dose required may be 5 to 20 times the usual dose. When nonselective beta-adrenoreceptor antagonists have been administered, large doses of isoprenaline are effective.[13] Isoprenaline in the dose which we used would be expected to cause marked vasodilatation and hypotension (beta$_2$ effect) before the inotropic effect becomes evident.[14,15] This may explain the increase in heart rate without increase in arterial blood pressure in our case.

When cardioselective beta-adrenoreceptor antagonists have been administered a pure beta$_1$ agonist, such as dobutamine, is effective. Intravenous calcium increases the inotropic state of the myocardium for short periods, while glucagon may increase it for longer periods.[13]

In contrast to the proven safety of anaesthesia and surgery in patients receiving propranolol,[16–18] there has been less experience with patients maintained on intermediate or long-acting beta-blockers such as atenolol or nadolol. It is now accepted that beta-adrenoreceptor blockers should be given on the morning of surgery. Whether they are short- or long-acting makes little difference if the operation lasts for only a couple of hours or less. Both short- and long-acting blockers will still be effective at the time of reversal of neuromuscular blockade. The recommendation that atenolol should be substituted by a short-acting beta-blocker prior to elective surgery, in order to avoid prolonged bradycardia and hypotension as a result of the interaction between a long-acting beta-blocker and neostigmine, may not therefore be justified.

References

1. Boudoulas H, Snyder GL, Karayannacos P, Vasko JS. Beneficial effect of continuation of propranolol through coronary bypass surgery. *Clinical Cardiology* 1979; **2:** 87–91.
2. Manners JM, Walters FJ. Beta-adrenoreceptor blockade and anaesthesia. Beta-adrenoreceptor antagonism during anaesthesia for coronary artery surgery. *Anaesthesia* 1979; **34:** 3–9.
3. Oka Y, Frishman W, Becker RM, Kadish A, Strom J, Matsumoto M, Orkin L, Frater R. Clinical pharmacology of the new beta-adrenergic blocking drugs. Part 10. Beta-adrenoreceptor blockade and coronary artery surgery. *American Heart Journal* 1980; **99:** 255–69.
4. Sprague DH. Severe bradycardia after neostigmine in a patient taking propranolol to control paroxysmal atrial tachycardia. *Anesthesiology* 1975; **42:** 208–10.
5. Prys-Roberts C. Hemodynamic effects of anesthesia and surgery in renal hypertensive patients receiving large doses of β-receptor antagonists. *Anesthesiology* 1979; **51:** S122.
6. Wagner DL, Moorthy SS, Stoelting RK. Administration of anticholinesterase drugs in the presence of beta-adrenergic blockade. *Anesthesia and Analgesia* 1982; **61:** 153–4.
7. Seidl DC, Martin DE. Prolonged bradycardia after neostigmine administration in a patient

taking nadolol. *Anesthesia and Analgesia* 1984; **63:** 365–7.

8. Owens WD, Waldbaum LS, Stephen CR. Cardiac dysrhythmia following reversal of neuromuscular blocking agents in geriatric patients. *Anesthesia and Analgesia* 1978; **57:** 186–90.
9. Heel RC, Brogden RN, Speight TM, Avery GS. Atenolol: a review of its pharmacological properties and therapeutic efficiency in angina pectoris and hypertension. *Drugs* 1979; **17:** 425–60.
10. Harry JD, Young J. The duration of action of atenolol in man. *British Journal of Clinical Pharmacology* 1977; **4:** 387P–8P.
11. Stiles GL, Taylor S, Lefkowitz RJ. Human cardiac beta-adrenergic receptors: sub-type heterogeneity delineated by direct radioligand binding. *Life Sciences* 1983; **33:** 467–73.
12. Bonelli J. Relevance of selectivity and non-selectivity in β-adrenoceptor blocking drugs. *British Journal of Clinical Pharmacology* 1982; **13** (Suppl. 2): 199S–200S.
13. Foëx P. Alpha- and beta-adrenoceptor antagonists. *British Journal of Anaesthesia* 1984; **56:** 751–65.
14. Waagstein F, Malek I, Hjalmarson A. The use of dobutamine in myocardial infarction for reversal of the cardiodepressive effect of metoprolol. *British Journal of Clinical Pharmacology* 1978; **5:** 515–21.
15. Hjalmarson A, Reiz S, Waagstein F. Possible antidotes to untoward effects of beta-blockers. In: Poppers PJ, van Dijk B, Elzakker AHMO, eds. *Beta-blockade in anaesthesia.* Rijswijk: Astra Pharmaceutica, 1980: 218.
16. Stoelting RK. Halothane–nitrous oxide anesthesia in a patient receiving high-dose propranolol. *Anesthesiology* 1979; **50:** 546–7.
17. Slogoff S, Keats AS, Ott E. Preoperative propranolol therapy and aortocoronary bypass operation. *Journal of the American Medical Association* 1978; **240:** 1487–90.
18. Kopriva CJ, Brown ACD, Pappas G. Hemodynamics during general anesthesia in patients receiving propranolol. *Anesthesiology* 1978; **48:** 28–33.

Anaesthesia, 1987, Volume 42, pages 1298–1301

CASE REPORT

Hypoglycaemic encephalopathy following surgery on phaeochromocytoma

A. B. CHANNA, A. B. MOFTI, G. W. TAYLOR, M. O. MEKKI AND M. H. SHEIKH

Summary

Severe hypoglycaemia as a complication of excision of a phaeochromocytoma has been reported seven times in the world literature. The eighth case, reported here, is unusual for the severity of the hypoglycaemic neurological damage which persisted for 10 weeks before ultimate recovery.

Key words

Complications; hypoglycaemic encephalopathy.
Surgery; phaeochromocytoma removal.

Many complications that follow surgery on phaeochromocytoma have been reported and mainly concern bleeding, haemodynamic disturbances, cardiac dysrhythmias and fluid balance problems. Phaeochromocytoma is also associated with a diabetic syndrome that presents with hyperglycaemia both pre- and postoperatively.

However, some patients may develop hypoglycaemia during surgery and immediately postoperatively, due to a rebound insulin storm as a result of inhibition of catecholamine secretion following removal of the tumour. Here we describe a case of hypoglycaemic encephalopathy that resulted from hypoglycaemia of nearly 4 hours' duration, which subsequently resolved without sequelae.

Case history

An 18-year-old Saudi male presented with intermittent attacks of severe headache, dizziness, palpitations and sweating that occurred over a period of 12 months. Blood pressure measurement during one such episode revealed severe hypertension and he was referred to King Khalid Hospital with a provisional diagnosis of phaeochromocytoma.

On examination he was a healthy young man of normal intelligence and behaviour. General and systematic examination revealed no abnormality. He remained normotensive apart from two brief elevations of arterial blood pressure to 170/90 mmHg.

A series of 24-hour urine samples showed elevation of vanillyl mandelic acid to three times the normal level. Ultrasonography and CT scan revealed a 5-cm mass in the right adrenal gland. The left adrenal was normal in size and shape. A diagnosis of phaeochromocytoma of the right adrenal gland was made and he was prepared for surgery with a 4-day course of phenoxy-

---

A.B. Channa, FFARCSI, A.B. Mofti, FRCS (Eng), FRCS (Glas), G.W. Taylor, FRCS (Eng), Professor, M.O. Mekki, MRCP (UK), M.H. Sheikh, FFARCS, King Khalid University Hospital, Department of Surgery (37), P.O. Box 2925, Riyadh 11461, Saudi Arabia.
Correspondence should be addressed to Dr A.B. Channa please.

0003–2409/87/121298 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

benzamine 10 mg twice daily. Because he did not have persistent hypertension or evidence of cardiac dysrhythmias, beta-adrenoreceptor blockade was not added to this regimen and he was deemed fit for surgery according to all the criteria described by Roizen.[1]

All other investigations were normal and both fasting and random blood sugar levels were within normal limits.

Anaesthetic management

He was premedicated with lorezepam 2 mg *nocte* and 3 mg orally, 1.5 hours before surgery. Anaesthetic induction was with droperidol 10 mg, thiopentone 250 mg, fentanyl 200 μg and atracurium 50 mg. His trachea was intubated after about 90 seconds and he was maintained with nitrous oxide–oxygen and enflurane 0.2–0.6%. Central venous pressure and intra-arterial lines were inserted. The patient had no cardiovascular abnormalities on intubation or positioning. Two brief bouts of hypertension occurred in the range of 180–190/110–120 mmHg during manipulation of the tumour. Blood pressure control was achieved by intermittent infusion of sodium nitroprusside. Persistent sinus tachycardia (120–150 beats/minute) was the main manifestation throughout the tumour dissection, for which propranolol 2.5 mg was administered in small increments.

Incremental doses of fentanyl up to 350 μg and atracurium 75 mg were also given as needed. The total duration of anaesthesia was 3 hours.

Operative procedure

Right adrenalectomy was performed through a posterior lumbotomy approach with resection of the 12th rib. The right pleural recess was opened during the resection and a water seal chest drain was inserted during closure of the wound.

The right adrenal gland contained a large, encapsulated, vascular tumour that measured 6 × 5 × 3 cm. Histological examination confirmed the diagnosis of phaeochromocytoma.

Intra-operatively he received 2 units of blood (800 ml), 500 ml Hartmann's solution and 300 ml 5% dextrose in saline. His total blood loss was approximately 500 ml. His central venous and arterial blood pressures were maintained within near normal limits throughout the procedure.

Postoperative course

Postoperatively, a lower thoracic epidural catheter was inserted for pain relief. The patient was then transferred to the surgical intensive care unit (ICU) for elective ventilation of the lungs (using a 900C Servovent) until he showed signs of recovery from anaesthesia.

In the ICU, 500 ml plasma were given fairly briskly and 5% dextrose in 0.45% saline, 3 litres, was prescribed for the next 24 hours. Blood sugar, urea, electrolytes and complete blood count were requested. However, the patient was inadvertently given Ringer's lactate instead of dextrose solution. A blood sugar estimation became available 4 hours after the patient was admitted to the ICU and showed a level of 1.9 mmol/litre. In view of this, 50 ml 50% dextrose were given intravenously and a 10% dextrose infusion was commenced and maintained thereafter. Subsequent blood sugar levels were between 5.7 and 9 mmol/litre but the patient remained stuporose and it was necessary to continue ventilation of the lungs. When attempts were made to wean the patient from the ventilator next morning, his breathing was adequate but response to vocal command was poor and he remained stuporose with sluggish response to painful stimuli. Both pupils were equal in size and reacted normally to light but he showed generalised exaggeration of reflexes and both plantar responses were extensor. No localising neurological signs were elicited.

A provisional diagnosis of hypoglycaemic encephalopathy was made and the trachea was re-intubated and the lungs ventilated. He was given dexamethasone 20 mg followed by 10 mg twice daily, and mannitol was given to lessen possible cerebral oedema. The $P\text{aco}_2$ was maintained at 25 mmHg and the patient was paralysed and ventilated for two more days. On the 4th postoperative day, after withdrawal of narcotics and muscle relaxants, he became conscious and obeyed commands. His trachea was then extubated. At this stage it was found that he had weakness (mild hemiparesis) of the right side of the body and an unequivocal Babinski response. Though rousable, he still had an irresistable desire to sleep and was also aphonic. He later developed a voracious appetite but his blood glucose level remained normal. He had a transient loss of memory and remained unresponsive to his environment. A CT scan showed an area of low attenuation in the anterior limb of the internal capsule on the left side and this was diagnosed as infarction of the area (Fig. 1). An EEG performed on two occasions was normal.

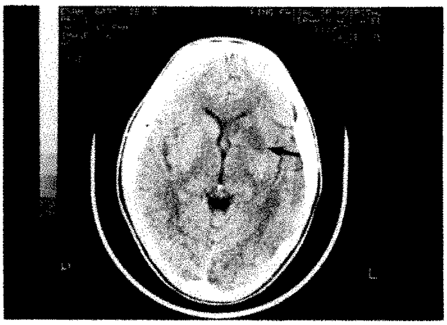


Fig. 1. CT scan: hypodense area of low attenuation (infarction) in the internal capsule area.

He made a slow recovery and one week later his speech and power on the right side were nearly normal but he remained mentally disoriented and unaware of his surroundings. This state improved slowly and he was eventually discharged home after a total of 4 weeks in the hospital and was asked to come to report in one month's time. His behaviour was quite normal on the second visit but he still had difficulty with mathematical problems. Two weeks later a CT scan was repeated and was reported as normal. His psychomotor skills and behaviour were also normal at this visit. Thus, he made complete recovery after 10 weeks following the hypoglycaemic episode.

Discussion

Hypoglycaemia following surgery for phaeochromocytoma removal has previously been reported in seven cases.[2-8] The main cause of this entity is the sudden withdrawal of tumour-produced catecholamines which promote glycogenolysis and have an inhibitory action on insulin in the form of its release and hypoglycaemic effect.[9-11] This effect can be offset after the catecholamine output is reduced following removal of phaeochromocytoma, with consequent rebound hyperinsulinism.[6] This has been well documented by a rapid rise of C-peptide levels after surgery.[7,8] Both C-peptide and insulin are secreted by beta-cells of the pancreas and exist in 1:1 molar proportion.[8] The constant catecholamine secretion by the tumour also depletes the glycogen store in the liver.[6] Thus, the ready conversion of glycogen to glucose in hypoglycaemic states is impaired.

Nonselective beta-blockers such as propranolol also impair glucose homeostasis in this circumstance. They produce hypoglycaemia by potentiation of the action of insulin[12] and prevention of the stimulation of glycogenolysis in the skeletal muscle.[13]

In our patient phenoxybenzamine 10 mg twice daily was used for 4 days only and no beta-blocker was administered pre-operatively. The 2.5 mg propranolol given intra-operatively might have masked the emerging signs and symptoms of hypoglycaemia as he was supported by artificial ventilation, and the 300 ml of 5% dextrose solution were probably insufficient to cope with a rebound insulin phenomenon. It has been recommended that blood glucose measurements should be repeated and glucose infusion should be continued in the first few hours postoperatively[6,8] until the insulin output is stabilised.

Hartmann's solution is known to increase the blood glucose level[14] but it is inefficient in protection against hypoglycaemia. Enflurane is protective against catecholamine-induced dysrhythmias but may augment hypoglycaemia after its withdrawal.[15] Encephalopathy due to hypoglycaemia may closely resemble an acute hypoxic insult[16] and may cause generalised or localised brain oedema, haemorrhagic exudates,[17,18] laminary cortical necrosis, destruction of corpus striatum and diffuse cellular changes in relatively less severely affected areas.[19] It is impossible to predict the outcome in such situations and some of the above-mentioned changes may be irreversible. The severity of the neurological insult is related directly to the degree and duration of the hypoglycaemia.[20,21]

In our patient, it is likely that the hypoglycaemia persisted for nearly 4 hours and blood glucose levels prior to the administration of 50 ml 50% glucose may have been lower than the level of 1.9 mmol/litre recorded. Subsequent administration of 10% dextrose solution which did not cause hyperglycaemia and glycosuria, is in favour of the occurrence of a rebound insulin state which is reported to require the administration of three times the normal glucose intravenously.[6,7]

In summary, a case of severe hypoglycaemic encephalopathy that followed excision of a phaeochromocytoma is described. It is suggested that blood glucose levels should be checked frequently in both the intra-operative and early postoperative period and that dextrose solutions should be the exclusive fluid therapy during this period.

Acknowledgment

We extend our gratitude to Mrs C. M. Fatayerji for typing the manuscript.

References

1. Roizen MF. Thyroid and parathyroid diseases, pheochromocytoma and diabetes mellitus: implications for the anesthetist. *34th Annual Refresher Course Lectures.* Atlanta: ASA Meeting, 1983.
2. Martin R, St-Pierre B, Moliner O. Phaeochromocytoma and postoperative hypoglycaemia. *Canadian Anaesthetists' Society Journal* 1979; **26:** 260–2.
3. Wilkins GE, Schmidt N, Doll WA. Hypoglycemia following excision of pheochromocytoma. *Canadian Medical Association Journal* 1977; **116:** 367–8.
4. Sagalowsky A, Donohue JP. Possible mechanism of hypoglycemia following removal of pheochromocytoma. *Journal of Urology* 1980; **124:** 422–3.
5. Allen CTB, Imrie D. Hypoglycemia as a complication of removal of a pheochromocytoma. *Canadian Medical Association Journal* 1977; **116:** 363–4.
6. Chambers S, Espiner EA, Donald RA, Nicholls MG. Hypoglycaemia following removal of phaechromocytoma: case report and review of the literature. *Postgraduate Medical Journal* 1982; **58:** 503–6.
7. Reynolds C, Wilkins GE, Schmidt N, Doll WA, Blix PM. Hyperinsulinism after removal of a pheochromocytoma. *Canadian Medical Association Journal* 1983; **129:** 349–53.
8. Meeke RI, O'Keeffe JD, Gaffney JD. Phaeochromocytoma removal and postoperative hypoglycaemia. *Anaesthesia* 1985; **40:** 1093–6.
9. Porte D Jr, Graber AL, Kuzuya T, Williams RH. The effect of epinephrine on immunoreactive insulin levels in man. *Journal of Clinical Investigation* 1966; **45:** 228–36.
10. Wilber JF, Turtle JR, Crane NA. Inhibition of insulin secretion by a phaeochromocytoma. *Lancet* 1966; **2:** 733.
11. Spergel G, Bleicher SJ, Ertel NH. Carbohydrate and fat metabolism in patients with pheochromocytoma. *New England Journal of Medicine* 1968; **278:** 803–9.
12. Lager I, Blohmé G, Smith U. Effects of cardioselective and non-selective beta-blockade on the hypoglycaemic response in insulin-dependent diabetics. *Lancet* 1979; **1:** 458–62.
13. Davies DM. *Textbook of adverse drug reactions,* 2nd edn. Oxford: Oxford Medical Publications, 1981: 324.
14. Thomas DJB, Albert KGMM. Hyperglycaemic effects of Hartmann's solution during surgery in patients with maturity onset diabetes. *British Journal of Anaesthesia* 1978; **50:** 185–8.
15. Oyama T, Matsuki A, Kudo M. Effects of enflurane (ethrane) anesthesia and surgery on carbohydrate and fat metabolism in man. *Anaesthesia* 1972; **27:** 179–84.
16. Himwich HE, ed. *Brain metabolism and cerebral disorders.* New York: Spectrum Publications Inc., 1976: 232–41.
17. Malamud N, Grosh IC. Hyperinsulinism and cerebral changes: report of a case due to an islet cell adenoma of the pancreas. *Archives of Internal Medicine* 1938; **61:** 579–99.
18. Sahs AL, Alexander L. Fatal hypoglycemia: a clinicopathologic study. *Archives of Neurology and Psychiatry* 1939; **42:** 286–97.
19. Courville CB. Vascular patterns of encephalic grey matter in man. *Bulletin of the Los Angeles Neurological Society* 1958; **23:** 30–43.
20. Mulder WD, Bastron JA, Lambert EH. Hyperinsulin neuronopathy. *Neurology* 1956; **6:** 627–35.
21. Rosner L, Elstad R. The neuropathy of hypoglycaemia. *Neurology* 1964; **14:** 1–6.

Anaesthesia, 1987, Volume 42, pages 1302–1305

CASE REPORT

Anaesthesia and septo-optic dysplasia

Implications of missed diagnosis in the peri-operative period

D. A. SHERLOCK AND L. R. McNICOL

Summary

Septo-optic dysplasia (De Morsier's syndrome) is a common cause of congenital optic nerve hypoplasia. Associated abnormalities such as hypothalamic/pituitary dysfunction, hypotonia or spasticity, may result in affected children presenting for surgical procedures under general anaesthesia. A 3.5-year-old boy with the undiagnosed condition had his Achilles tendons elongated under an uncomplicated general anaesthetic. The postoperative period was complicated by coma and a major convulsive seizure which responded to glucose and steroids. The importance of awareness of this condition in short children with poor visual acuity who require general anaesthesia is stressed, and the presenting features of seven other cases are demonstrated.

Key words

Co-existing disease; septo-optic dysplasia, De Morsier's syndrome.
Complications; coma, convulsions.

Septo-optic dysplasia (De Morsier's syndrome) is a congenital neurological disorder that is now recognised more frequently and, indeed, may be the commonest cause of congenital optic nerve hypoplasia. The syndrome comprises optic nerve hypoplasia, absence or abnormality of the septum pellucidum with associated mid-brain anomalies and/or hypothalamic/pituitary dysfunction. Other features, such as delayed motor development, spastic quadriparesis, corticospinal tract involvement, hypotonia or generalised clumsiness may also be present. Children with septo-optic dysplasia are not infrequently subjected to surgery for correction of orthopaedic deformities or other congenital abnormalities associated with the syndrome, as well as for trauma and incidental surgical emergencies such as appendicitis. When pituitary dysfunction is present this can complicate anaesthesia, especially if the syndrome is not recognised pre-operatively. We present a case history to illustrate this point and review seven other cases of septo-optic dysplasia to demonstrate the variability of presentation.

Case history

The child, a male, weight 2.68 kg, was born at term by spontaneous vertex delivery. In the neonatal period he was mildly jaundiced and required four 12-hour periods of phototherapy. The child was noted to be floppy and required regular dextrose feeds to correct hypoglycaemia during the first 2 weeks of life. He was soon recognised to have developmental retardation associated with a mild spastic quadriplegia and

---

D.A. Sherlock, DPhil, FRCS, Senior Registrar in Orthopaedics, L.R. McNicol, FFARCS, Consultant, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ.
Correspondence should be addressed to Dr L.R. McNicol please.

0003–2409/87/121302 + 04 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

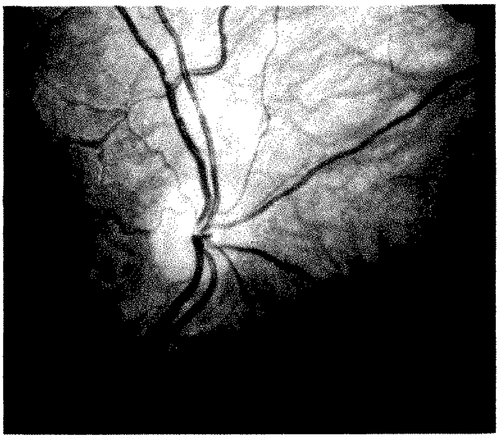


Fig. 1. Photograph of retina demonstrating the typical double ring appearance of a hypoplastic optic disc.

blindness with no detectable visual following although he exhibited a coarse searching nystagmus. His pupils reacted slowly and fundoscopy revealed small, pale optic discs (Fig. 1). Virological studies excluded congenital rubella, cytomegalovirus, toxoplasma and herpes as the cause of his neurological problems. Hearing tests revealed some abnormalities but he was not deaf.

At age 3.5 years he was referred for an orthopaedic opinion because of increasing bilateral equinus deformities of his ankles which interfered with walking. Bilateral tendo Achilles lengthening was subsequently carried out under general anaesthesia which consisted of premedication with oral droperidol and diazepam, gaseous induction and maintenance with halothane in nitrous oxide and oxygen. Pentazocine 7.5 mg was titrated intravenously and he breathed spontaneously. Total anaesthetic time was 40 minutes and no intravenous fluids were administered intra-operatively. His immediate postoperative recovery was unremarkable. However, he remained very sleepy, refused oral fluids and eventually became barely rousable. One short convulsive seizure was noted which did not require anticonvulsant therapy. No focal neurological signs were detected but an immediate Dextrostix test revealed hypoglycaemia which was treated initially by 10 ml 50% dextrose and then an intravenous infusion of dextrose. This brought about a slow improvement in his conscious level but he remained lethargic despite normoglycaemia. A neurological opinion was sought, at which point the diagnosis of septo-optic dysplasia was first entertained. Treatment with hydrocortisone was commenced and resulted in a return to normal consciousness. His subsequent postoperative recovery was uncomplicated.

Investigation of his hypothalamic/pituitary axis by an insulin tolerance test showed an adequate cortisol response (peak level 2.6 times basal level) although the peak of 19.0 μg/litre was in the low normal range despite a hypoglycaemia of 0.9 mmol/litre. The growth hormone response to this hypoglycaemia was deficient; it reached only 3.3 mU/litre (normal 15 mU/litre) 30 minutes after the glucose level had reached its nadir. Luteinising hormone (LH), follicle stimulating hormone (FSH) and thyroid stimulating hormone (TSH) all responded adequately. Direct stimulation of the pituitary by prostaglandin unexpectedly produced subnormal cortisol and growth hormone responses. This result was possibly invalid because fasting prior to the procedure had produced hypoglycaemia (0.8 mmol/litre falling to 0.4 mmol/litre) thereby providing pre-existing hypothalamic stimulation. These investigations confirmed dysfunction of the hypothalamic/pituitary axis and are consistent with the mid-line cephalic anomalies commonly found in septo-optic dysplasia.

The growth hormone deficiency has since been confirmed by his growth velocity: his height has remained below the third percentile (birth length 46 cm, height at 4 years 91 cm, height at 12 years 121 cm), as also has his weight. A CT scan performed at age 9 years showed absence of the septum pellucidum, with abnormal anterior lateral ventricular horns and slight dilatation of the bodies of the lateral ventricles. This provides anatomical confirmation of the diagnosis of septo-optic dysplasia.

Discussion

The association between congenital optic hypoplasia and absence of the septum pellucidum on pneumoencephalography was first described by Reeves[1] in 1941. De Morsier[2] named the syndrome septo-optic dysplasia in 1956 when he reported postmortem findings in nine cases with the features. The full syndrome was described in 1970 by Kaplan *et al.*[3] who presented six patients with pituitary hormone deficiency, optic

Table 1. Cases of septo-optic dysplasia.

Clinical features	Height percentile	Weight percentile	Endocrine assessment and treatment	Operations	CT
Marked mental and motor retardation, spastic quadriparesis, optic hypoplasia *	<3	<3	ACTH↓, GH↓ Occasional hydrocortisone	ETA	SP absent
Marked mental and motor retardation, fits, optic hypoplasia	<3	<3	ACTH↓↓, GH↓↓ Hydrocortisone + GH	CT scan under GA	SP absent
Delayed development, salaam fits, mild spasticity, optic hypoplasia	<3	<50	ACTH↓↓, ?GH↓ Hydrocortisone	None	SP absent
Moderate delay in motor development, optic hypoplasia	<3	<3	ACTH↓↓, GH↓↓ Hydrocortisone + GH	None	SP absent
Fits, right optic hypoplasia	50	75	ACTH↓, GH↓	Pyloromyotomy	Normal SP
Scoliosis, optic hypoplasia	<3	<3	ACTH↓↓, GH↓↓, T4↓↓ Hydro-cortisone + GH + T4	No	SP absent
Global delay and hypothalamic dysfunction, giant cell hepatitis, optic hypoplasia (died age 17 months)	—	<3	Panhypopituitarism	No	Air encephalogram normal
Left hemiparesis, severe mental handicap, fits, optic hypoplasia	10	10	ACTH↓↓, T4↓↓, ADH↓↓ Hydro-cortisone + T4 + desmopressin Precocious puberty	None	SP absent

* Subject of case report. ETA, Elongation of tendo Achillis; CT, computer tomography of brain; SP, septum pellucidum; GA, general anaesthetic; ACTH, adrenocorticotrophic hormone; GH, growth hormone; T4, thyroxin; ADH, antidiuretic hormone.

nerve hypoplasia and mid-line abnormalities of the prosencephalon.

There is a wide variability in the clinical picture.[4] Classically the patient presents with defective visual acuity, often congenital nystagmus, and small stature. Some patients may have almost no neurological deficit and normal intelligence while others may have severe retardation of motor and mental developmental and/or spastic quadriparesis. Seizures occur in some with either focal or diffuse EEG changes. Hypopituitarism may become apparent at any age, although early onset is most common. Recurrent hypoglycaemia may produce further brain damage and aggravate pre-existing disabilities.

The surgeon or anaesthetist faced with a child who requires surgery and has reduced or absent visual acuity and small stature, does not have an easy task in identifying septo-optic dysplasia. Optic disc hypoplasia, the *sine qua non* of septo-optic dysplasia, may be hard to visualise in the presence of nystagmus unless sedation or a general anaesthetic is risked. Pituitary hormone levels may be normal in the non-stress situation. A CT examination of the brain is not foolproof since septo-optic dysplasia occurs with the normal septum pellucidum as visualised by CT.[5] A history of jaundice and hypoglycaemic fits in the neonatal period, or of fits in later childhood in response to illness, is helpful but full assessment of the hypothalamic/pituitary axis may be necessary to establish the diagnosis.

At the Royal Hospital for Sick Children in Glasgow a further seven cases of septo-optic dysplasia have been identified (Table 1). Another 22 children have optic hypoplasia with normal pituitary function and may, in time, develop the full picture of septo-optic dysplasia. Of the eight cases of septo-optic dysplasia three have required operations. The case above was the only one not diagnosed pre-operatively and covered with hydrocortisone and intravenous fluids, and complications developed as a result. One patient with severe septo-optic dysplasia has died from intercurrent infection.

Conclusion

Septo-optic dysplasia (De Morsier's syndrome) is now diagnosed with increasing frequency as clinicians become aware of it. Anaesthesia in known cases may have to include peri-operative steroid therapy and care should be taken to avoid hypoglycaemia. Undiagnosed children may present for general anaesthesia and the surgeon and anaesthetist should be aware that small children with poor visual acuity, spasticity, and perhaps a history of seizures, may present a peri-operative risk.

Acknowledgment

We thank Dr J. B. P. Stephenson, Consultant Neurologist, for his cooperation in the preparation of this paper.

References

1. Reeves DL. Congenital absence of the septum pellucidum. *Bulletin of the Johns Hopkins Hospital* 1941; **69:** 61–71.
2. De Morsier G. Études sur les dysraphies crânio-encéphaliques. III. Agénésie du septum lucidum avec malformation du tractus optique; la dysplasie septo-optique. *Schweizer Archiv für Neurologie und Psychiatrie* 1956; **77:** 267–92.
3. Kaplan SL, Grumbach MM, Hoyt WF. A syndrome of hypopituitary dwarfism, hypoplasia of optic nerves and malformation of the prosencephalon: report of 6 patients (Abstract). *Pediatric Research* 1970; **4:** 480–1.
4. Morishima A, Aranoff GS. Syndrome of septo-optic–pituitary dysplasia: the clinical spectrum. *Brain and Development* 1986; **8:** 233–9.
5. Stanhope R, Preece MA, Brook CGD. Hypoplastic optic nerves and pituitary dysfunction. A spectrum of anatomical and endocrine abnormalities. *Archives of Disease in Childhood* 1984; **59:** 111–4.

Anaesthesia, 1987, Volume 42, pages 1306–1307

CASE REPORT

Displacement of a minitracheotomy tube during high frequency jet ventilation

A. RAVALIA AND M. A. STOCKWELL

Summary

A patient required respiratory support with jet ventilation via a minitracheotomy tube 2 days after right upper lobectomy. After initial improvement, the patient's condition deteriorated because of migration of the minitracheotomy tube out of the larynx. This complication has not been described previously. A number of possible causative factors and remedies are discussed.

Key words

Complications; displacement of minitracheotomy tube.
Ventilation; high frequency jet ventilation.

Transtracheal ventilation has become an accepted technique since its description by Spoerel *et al.*[1] Since its use via a minitracheotomy was described first by Mathews *et al.*,[2] a variety of hazards have been described.[3] We report a case of displacement of a minitracheotomy tube during high frequency jet ventilation (HFJV).

Case history

Two days after a right upper lobectomy, a 70-year-old woman developed respiratory failure which was presumed to be the result of sputum retention. Results of blood gas analysis at this time were pH 7.27, $Paco_2$ 7.8 kPa, Pao_2 11.7 kPa while she breathed 40% oxygen. Initial treatment with doxapram by infusion and physiotherapy proved to be ineffective and her blood gases deteriorated (pH 7.16, $Paco_2$ 10.8 kPa, Pao_2 7.3 kPa). A minitracheotomy (Minitrach 2, Portex) was performed to facilitate suction of the airway and the position of the tube was confirmed on an anteroposterior chest X ray.

Her condition failed to improve and high frequency jet ventilation (HFJV) was instituted via the minitracheotomy, using an Acutronic ventilator. A modified connector was used to ventilate the lungs directly via the minitracheotomy tube, without a jet catheter. The modification consisted of fixing a metal female Luer connector to the standard Acutronic T-piece which is designed to fit the 15-mm connector of a tracheotomy or oral tracheal tube. This enables the jet system to be used without a catheter. Oxygen was delivered at a driving pressure of 2.1 bar and a rate of 200 breaths/minute using the first catheter power selection position which is designed for delivery of jet ventilation through a 14-gauge jet cannula. There was an appreciable improvement in the patient's clinical condition and in her blood gases (pH 7.28, $Paco_2$ 8.8 kPa, Pao_2 34.0 kPa).

A. Ravalia, MB, ChB, FFARCS, M.A. Stockwell, MB, BS, FFARCS, Registrars, Department of Anaesthetics, St. George's Hospital, Blackshaw Road, Tooting, London.

0003–2409/87/121306 + 02 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

Her clinical condition deteriorated 24 hours later despite acceptable blood gases (pH 7.41, $Pa\text{CO}_2$ 6.7 kPa, $Pa\text{O}_2$ 11.2 kPa) on 50% oxygen. Suction applied through a catheter passed down the minitracheotomy tube produced yellow, acid fluid; the abdomen was noted to be distended and resonant. Jet ventilation was stopped but further clinical deterioration with tachycardia and tachypnoea led to the decision to remove the minitracheotomy and to intubate the trachea with an oral tracheal tube. At laryngoscopy, the minitracheotomy tube was found to pass up between the vocal cords and curl down into the oesophagus. Jet ventilation was re-instituted via a Mallinckrodt Hi-Lo tube with the jet ventilator set at a driving pressure of 1.2 bar and a rate of 150 breaths/minute; the resulting blood gases were pH 7.5, $Pa\text{CO}_2$ 3.9 kPa, $Pa\text{O}_2$ 19.5 kPa and there was considerable improvement in her clinical condition. Subsequently, a paralysed right hemi-diaphragm was discovered as the cause of respiratory failure.

No sequelae attributable to the misplacement have occurred.

Discussion

The application of HFJV via a minitracheotomy is becoming common practice in many units and preliminary reports suggest that it has many advantages.[3] This case illustrates a novel hazard which might have proved fatal had the patient's respiratory failure been more profound.

The failure of the technique in our patient could be ascribed to the lack of a purpose-designed jet minitracheotomy tube, softening of the tube at body temperature or expulsive forces that resulted from the patient coughing.

The normal jet catheter supplied with the ventilator is a modified intravenous cannula with side holes to provide stability and to reduce whipping of the tip under the force of the jet. In view of the fact that the minitracheotomy tube lies free in the airway, some consideration of the mobility of the tube must be made when the technique of HFJV is modified and applied to minitracheotomies. Possible solutions include manufacture using a stiffer material, the incorporation of side holes at the distal end or ventilation through a metal cannula passed through the minitracheotomy tube; however, the last of these might carry risks of tracheal perforation.

References

1. SPOEREL WE, NARAYANAN PS, SINGH NP. Transtracheal ventilation. *British Journal of Anaesthesia* 1971; **43:** 932–8.
2. MATHEWS HR, FISCHER B, HOPKINSON RB. Minitracheotomy and jet ventilation: a new method of ventilatory support. *Thorax* 1984; **39:** 688.
3. FISCHER HBJ, SMITH BE. High frequency ventilation. In: DELARUE NC, ESCHAPASSE H, eds. *International trends in general thoracic surgery, Vol. I. Lung cancer.* Philadelphia: W.B. Saunders, 1985: 207–16.

Anaesthesia, 1987, Volume 42, pages 1308–1312

APPARATUS

Potential leaks from anaesthetic machines

Potential leaks through open Rotameter valves and empty cylinder yokes

P. J. McQUILLAN AND I. J. B. JACKSON

Summary

Twenty anaesthetic machines were examined to detect leakage of fresh gas through open Rotameter flow control valves and empty cylinder yokes. Significant leakage was demonstrated in most machines. Any leakage in machines which comply with ISO 5358, where oxygen is the last gas into the common gas manifold, is selective for nitrous oxide and, conversely, it is selective for oxygen in machines where oxygen is the first gas into the common gas manifold. Leakage is augmented by back pressure from ventilators that function as minute volume dividers. In ventilated patients the leakage described may contribute to hypoventilation and patient hypoxia or to pollution of the operating theatre and patient awareness.

Key words

Equipment; anaesthetic machines, Rotameters.

The potential leakage of gas through the cyclopropane Rotameter and empty yoke has been known for many years[1,2] and, indeed, has been used as a controllable leak when leak tests are described. Wilson and Burleton[1] simulated a leak at this site and believed that the leak occurred 'since neither reducing nor back check valves are present for this gas.'

It has also long been known that leaks may occur through any Rotameter/yoke system when the flow control valves are open in combination with the absence of either a cylinder or a yoke blank. It is widely believed that such leaks, which may occur in spite of a pressure regulator and a unidirectional valve,[3] are of minor importance. However, we could find no evidence to support this. We therefore tested our anaesthetic machines to record these leaks.

Methods

Twenty anaesthetic machines were examined including five Boyle 2000 machines, five Boyle International machines, four Cavendish 500 MIE machines and six Gardner 200 machines. The Boyle 2000 machines have Rotameters for air and carbon dioxide in addition to oxygen and nitrous oxide; the remaining machines have carbon dioxide Rotameters only. A further four machines examined (one Boyle KL, three Gardner 1000) incorporate cyclopropane Rotameters. All machines are in constant use in our theatres. They are between 2 and 15 years old and are serviced every 3 months by the manufacturers or our anaesthetic technicians.

Measurements were made of oxygen concentration delivered at the common gas outlet or at the outlet of a Manley Pulmovent, for gas

---

P.J. McQuillan, FFARCS, Registrar, I.J.B. Jackson, FFARCS, Senior Registrar, Department of Anaesthesia, Newcastle General Hospital, Westgate Road, Newcastle-upon-Tyne NE4 6BE.

Correspondence should be addressed to Dr I.J.B. Jackson please.

0003–2409/87/121308 + 05 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

flows of 6 litres/minute nitrous oxide and 3 litres/minute oxygen. Two oxygen analysers were employed: a Critikon Oxycheck and a Teckmar T25. These instruments were calibrated using ambient air and 100% oxygen. Minor adjustments were made to the Rotameters to produce an oxygen concentration of 33% in the fresh gas flow and they were then left undisturbed.

Potential leaks were then introduced by removal of all yoke blanks and all cylinders, except oxygen and nitrous oxide, and opening fully the carbon dioxide, air or cyclopropane Rotameters individually and then in combination. A Manley Pulmovent MPP ventilator was employed to produce back pressure and to measure the effect on gas leakage and, hence, oxygen concentration at the common gas outlet.

The technique described by Page[4] was subsequently employed, in which the machine common gas outlet is connected to a pressure gauge, the oxygen valve is slowly opened and adjusted to maintain a pressure of 16 kPa (120 mmHg) at the common gas outlet. The oxygen flow measured in this way is an indication of the leakage; more than 200–300 ml/minute is considered unacceptable[4] (this procedure does not measure the absolute leak flow under working conditions).

Statistical analysis was performed using the Wilcoxon signed rank test for nonparametric data.

Results

The results are shown in Tables 1–4. The Boyle International, Cavendish 500 MIE and Gardner 200 machines, where oxygen is the first gas into the common gas manifold, showed decreases in oxygen concentration. Augmentation of the leakage occurred with a Manley Pulmovent and the minimum oxygen concentrations recorded were 22% in a Boyle International and 19% in a Gardner 200 machine.

In Boyle 2000 machines oxygen enters the common gas manifold downstream of other

Table 1. Measurements on five Boyle International machines.

	Oxygen concentration,* %	Oxygen flow,† ml/minute
No leakage (carbon dioxide Rotameters closed)		
Mean (range)	33	132 (100–200)
Median	33	125
Leak via carbon dioxide pathway		
Mean (range)	32.1 (31–33)	1105 (850–1300)
Median	32	1175
Leak via carbon dioxide pathway augmented by Manley Pulmovent		
Mean (range)	24.2 (22–27)	—
Median	23	

* At Rotameter settings of 6 litres/minute nitrous oxide and 3 litres/minute oxygen.
† Flow required to maintain a common gas outlet pressure of 16 kPa (120 mmHg).

Table 2. Measurements on three Cavendish 500 MIE machines.

	Oxygen concentration,* %	Oxygen flow,† ml/minute
No leakage (carbon dioxide Rotameters closed)		
Mean (range)	33	100 (50–200)
Median	33	125
Leak via carbon dioxide pathway		
Mean (range)	32 (31–33)	508 (350–600)
Median	32	575
Leak via carbon dioxide pathway augmented by Manley Pulmovent		
Mean (range)	28.7 (26–32)	—
Median	28	

* At Rotameter settings of 6 litres/minute nitrous oxide and 3 litres/minute oxygen.
† Flow required to maintain a common gas outlet pressure of 16 kPa (120 mmHg).

Table 3. Measurements on six Gardner 200 machines.

	Oxygen concentration,[*] %	Oxygen flow,[†] ml/minute
No leakage (carbon dioxide Rotameters closed)		
Mean (range)	33	163 (50–450)
Median	33	200
Leak via carbon dioxide pathway		
Mean (range)	31.1 (26–33)	580 (50–1700)
Median	30	600
Leak via carbon dioxide pathway augmented by Manley Pulmovent		
Mean (range)	29.6 (19–33)	—
Median	27	

[*] At Rotameter settings of 6 litres/minute nitrous oxide and 3 litres/minute oxygen.
[†] Flow required to maintain a common gas outlet pressure of 16 kPa (120 mmHg).

Table 4. Measurements on five Boyle 2000 anaesthetic machines.

	Oxygen concentration,[*] %	Oxygen flow,[†] ml/minute
No leakage (carbon dioxide Rotameters closed)		
Mean (range)	33	70 (50–100)
Median	33	75
Leak via carbon dioxide pathway		
Mean (range)	37.8 (37.0–39.5)	1270 (350–1750)
Median	38	1300
Leak via carbon dioxide pathway augmented by Manley Pulmovent		
Mean (range)	40.2 (37.0–45.0)	
Median	39.5	
Leak via air pathway		
Mean (range)	38.8 (36.5–43.0)	1650 (800–3800)
Median	39	1300
Leak via air pathway with Manley Pulmovent		
Mean (range)	42.8 (37.5–56.0)	
Median	40.25	
Leak via carbon dioxide and air pathways		
Mean (range)	42.0 (40.0–46.0)	2900 (1100–5000)
Median	44	2700
Leak via carbon dioxide and air pathways with Manley Pulmovent		
Mean (range)	52.1 (42–68.5)	—
Median	51	

[*] At Rotameter settings of 6 litres/minute nitrous oxide and 3 litres/minute oxygen.
[†] Flow required to maintain a common gas outlet pressure of 16 kPa (120 mmHg).

gases and oxygen concentration was increased with open leakage pathways. In one particular Boyle 2000 machine, a dual carbon dioxide and air leakage pathway augmented by a Manley Pulmovent produced an oxygen concentration of 68.5% instead of the intended 33%.

Three Cavendish 500 MIE machines produced leaks with decreases in oxygen concentration (Table 2). The leakage in a fourth machine produced an increase in oxygen concentration to 34%, augmented to 36% with the Manley Pulmovent. The test flow value increased from 50 to 600 ml/minute. It was discovered that this machine had a new Rotameter block in which oxygen entered the common gas manifold downstream of the other gases.

Of the four machines with cyclopropane Rotameters, leaks were demonstrable in the Boyle KL and one Gardner 1000 machine. Oxygen enters the common gas manifold first and oxygen concentrations were reduced to minima of 31.5% and 27% by the Manley Pulmovent and the test flow values increased from 130 and 250 to 400 and 800 ml/minute, respectively.

Discussion

A bobbin at the bottom of a Rotameter indicates no gas flow but it does not produce a gas-tight seal and reversed gas flow is possible if there is an open leakage pathway through an empty cylinder yoke. The carbon dioxide, air and cyclopropane Rotameters lie between the oxygen and nitrous oxide Rotameters in the Rotameter blocks tested. The leakage route in machines in which oxygen is the first gas into the common gas manifold, is downstream of oxygen but upstream of nitrous oxide and, thus, the leakage is selective for oxygen. This reduces oxygen concentration and total fresh gas flow, although the latter was not measured. The lowest oxygen concentration, 19%, represents a calculated oxygen loss of 1590 ml/minute if the leaking gas is assumed to be pure oxygen. This shortfall in oxygen concentration may cause patient hypoxia and the decreased fresh gas flow may produce hypoventilation and hypercapnia.

The leakage in machines in which oxygen enters the common gas manifold downstream of other gases, as recommended by ISO 5358,[5] is selective for nitrous oxide and results in increased oxygen concentration and diminished total fresh gas flow. The mean and maximum oxygen concentrations for the Boyle 2000 machines with dual carbon dioxide and air leakage pathways augmented by the Manley Pulmovent, 52% and 68.5%, respectively, represent calculated nitrous oxide losses of 3230 and 4620 ml/minute. Patients may thus be at risk of awareness and hypoventilation. These leaks are audible on most machines but might readily be missed in a noisy theatre.

The above leaks were demonstrated on several makes of anaesthetic machine via the carbon dioxide, air and cyclopropane pathways. Furthermore, leakage may be demonstrated via an open nitrous oxide leakage pathway by use of 2 litres/minute carbon dioxide and 1 litre/minute oxygen. Boyle 2000 machines may leak through the carbon dioxide and air pathways; in fact, our Boyle 2000 machines may be made to leak if the air Rotameter is open even in the absence of an air cylinder yoke.

These leaks occur in spite of a pressure regulator and a unidirectional valve. The unidirectional valves, which consist of a bobbin and O ring, are designed to function at high pressures. The low flow, low pressure leaks described above are insufficient to close these valves.

Leakage of fresh gas may thus occur through any open Rotameter valve to an empty cylinder yoke. Such leaks may be augmented by back pressure produced by ventilators that function as minute volume dividers. Using the Wilcoxon signed rank test the leaks through the open carbon dioxide pathways were highly significant ($p < 0.0004$).

The protocols for single hose tests[6,7] begin by opening all flow control valves but they fail specifically to recommend that they should all be turned off at the end. This is a small but significant omission, since failure to do so may produce a variable leak and alteration in the oxygen concentration of fresh gas, and thus expose the patient to an increased risk of hypoxia or awareness and hypoventilation.

It is the responsibility of the anaesthetist to check the machine thoroughly[8] and to ensure that all flow control valves not in use are turned off. It has been recommended that all empty cylinder yokes are fitted with a yoke blank.[9] In-line oxygen analysers provide a final safeguard.

A *Health Devices Alert*[10] was produced following the report of Williams and Hilton[2] about leakage through the cyclopropane pathway. Ohmeda has agreed to supply all users of its machines with yoke blanks.

Acknowledgments

We are grateful to Drs N.M. Heggie and M.A. Stafford and Mr D. Thornton for their help and support in preparing this paper.

References

1. WILSON ME, BURLETON AS. Leak tests. *British Journal of Anaesthesia* 1982; **54:** 572.
2. WILLIAMS AR, HILTON PJ. Selective oxygen leak. A potential cause of patient hypoxia. *Anaesthesia* 1986; **41:** 1133–4.
3. WARD CS. *Anaesthetic equipment*, 2nd edn. London: Baillière Tindall, 1985: 107–9.
4. PAGE J. Testing for leaks. *Anaesthesia* 1977; **32:** 673.

5. *International standard ISO 5358 1980(E)*. Continuous flow inhalational anaesthetic apparatus (anaesthetic machines) for use with humans. Geneva: International Organization for Standardisation, 1980: para 11.5.
6. CUNDY J, BALDOCK GJ. Safety check procedures to eliminate faults in anaesthetic machines. *Anaesthesia* 1982; **37**: 161–9.
7. MARSHALL RD. The 'single hose' or 'qualitative' test and nitrous oxide cut off devices. *Anaesthesia* 1978; **33**: 639.
8. LUNN JN. The law and the practice of anaesthesia. *Anaesthesia* 1986; **41**: 1085.
9. DORSCH JA, DORSCH SE. *Understanding anaesthetic equipment*, 1st edn. Baltimore: Williams and Wilkins, 1975: 27.
10. EMERGENCY CARE RESEARCH INSTITUTE. *Health Devices Alert* 1986; **10**: 23.

Anaesthesia, 1987, Volume 42, pages 1313–1315

Forum

Arterial oxygen desaturation during postoperative transportation: the influence of operation site

B. H. Meiklejohn, BSc, MB, ChB, FFARCS, Lecturer, G. Smith, MD, FFARCS, Professor of Anaesthesia, A. E. Elling, RGN, Research Nurse, N. Hindocha, HNC, Medical Physics Technician, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

Summary

Arterial oxygen saturation in 132 patients was measured using a Biox IV oximeter with an ear probe, during transfer from theatre to recovery room following a variety of surgical procedures. Oxygen saturation decreased to 85% or less in 21.9% of patients and to 90% or less in 61.4%. No predictive factors were identified. It is recommended that supplementary oxygen be given to all patients in the immediate postoperative period, including the period of transit to the recovery room.

Key words

Hypoxia, postoperative.
Measurement techniques; pulse oximetry.

Hypoxia in the immediate postoperative period has been a matter of concern for a number of years. Many factors may be involved in this process, including hypoventilation, diffusion hypoxia, imbalance of ventilation and perfusion (V/Q), atelectasis and increased oxygen demand as a result of postanaesthetic shivering.

Two recent developments have highlighted this problem. First, the building of large theatre complexes with a central recovery area has the result that patients are often transported without supplementary oxygen for relatively long distances from the operating theatre to the recovery area. Second, the introduction of pulse oximeters into clinical practice has provided a convenient, noninvasive method for continuous monitoring of arterial oxygen saturation (Sao_2) both intra- and postoperatively (including periods in transit). Using this technique, Tyler *et al.*[1] showed that Sao_2 decreases significantly in a large number of patients transported without supplementary oxygen from the operating theatre to the recovery area.

It is well known that in the later postoperative period (6–36 hours), arterial oxygenation is significantly lower in patients following upper abdominal than lower abdominal surgery[2] and in the obese compared with the nonobese patient.[3] However, there are few published data on this comparison in the early postoperative period. The present study was initiated at the same time as that of Tyler and was designed to examine if Sao_2 in the immediate postoperative period (10 minutes) is affected by the site of operation.

Patients and methods

The study was conducted in the Central Operating Department of Leicester Royal Infirmary. The distance between the theatres and the recovery area in this complex varies between 30 and 80 metres and the transit time was found to range from 90–240 seconds in a preliminary study of 30 patients. Adult patients scheduled to undergo surgical procedures under general anaesthesia were studied. Patients with severe respiratory or cardiac disease were excluded. The patient's age, sex and pre-operative cardiac and respiratory status were recorded together with details of the surgery and anaesthetic technique used. The duration of administration of 100% oxygen at the end of anaesthesia was also noted.

Sao_2 was measured using the Biox IV oximeter with an ear probe, pre-operatively, during stable anaes-

0003–2409/87/121313 + 14 $03.00/0 © 1987 The Association of Anaesthetists of Gt Britain and Ireland

thesia and during the period from removal of the anaesthetic facemask or tracheal tube, until the patient was settled in the recovery room. Measurements exhibited on the oximeter were recorded at 30-second intervals. Because this study was intended to investigate oxygenation in current practice, neither the anaesthetist nor recovery nurse was informed of the values of $Sa\text{O}_2$ recorded unless profound hypoxia was present.

Patients were classified according to the operation and the mode of ventilation as follows:

Group I: peripheral operations, spontaneous ventilation (SV);
Group II: peripheral operations, artificial ventilation (IPPV);
Group III: lower abdominal operations, SV;
Group IV: lower abdominal operations, IPPV;
Group V: upper abdominal operations, IPPV.

Saturation values of 90% or less were classified as hypoxia, and of 85% or less as severe hypoxia. These values correspond to approximate $Pa\text{O}_2$ values of 7.7 and 6.6 kPa, respectively.

The data were analysed statistically using Students' *t*-test and the Chi-squared test with Yates' correction for small numbers.

Results

Sixty-one male and 71 female patients were studied. Details of age, duration of operation and the duration of administration of 100% oxygen at the end of anaesthesia are shown in Table 1.

Overall, 81 patients (61.4%) were hypoxic and 29 (21.9%) severely hypoxic at some time in transit between the operating theatre and recovery room. The lowest mean $Sa\text{O}_2$ for all groups was 88.63% which occurred between 30 and 540 seconds (mean 221 seconds) following removal of the mask or tracheal tube.

The incidence of hypoxia was similar in all groups but severe hypoxia was seen in 34.4% of group V patients compared to 19%, 20.8%, 15% and 14.3% for groups I–IV, respectively (Table 2). This is not statistically significant in the numbers studied but if this trend were to continue, extrapolation suggests that significance would be reached after a further 50–60 patients in group V. It was, however, considered unethical to continue the study with this incidence of severe hypoxia and oxygen has now been made available for use in transit.

There was no significant difference in the incidence or degree of desaturation as a function of age, duration of anaesthesia, duration of oxygenation or pre-operative $Sa\text{O}_2$ (data analysed by regression analysis for each group and for total pooled data).

The patients of one anaesthetist who used a trichloroethylene–halothane technique with 100% oxygen with a drawover vaporizer, were matched for age, sex and operation with patients who received a nitrous oxide–oxygen–volatile agent technique. There was no difference in the incidence or degree of desaturation between the patients subjected to the two techniques.

Discussion

The results of this study have confirmed previous findings that significant arterial desaturation is a common phenomenon in the immediate postoperative period. The degree of desaturation did not correlate with the patient's age, duration of anaesthesia or administration of 100% oxygen, or the anaesthetic

Table 1. Patient data.

	Patient age, years		Duration of surgery, minutes		Duration of administration of 100% oxygen at termination of anaesthesia, minutes	
Group	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
I ($n = 42$)	43.1 (16.9)	10–77	43.8 (26.2)	10–110	85.9 (95.4)	0–360
II ($n = 24$)	54.3 (17.6)	22–78	88.0 (44.1)	30–185	190.0 (137.1)	45–600
III ($n = 20$)	46.7 (18.9)	16–77	46.2 (30.3)	20–130	65.9 (88.2)	0–165
IV ($n = 14$)	50.2 (17.9)	18–75	46.9 (19.7)	21–85	138.9 (89.6)	0–220
V ($n = 32$)	61.2 (13.8)	30–81	104.0 (54.8)	24–225	216.9 (118.7)	14–600

Table 2. Incidence of desaturation.

Group	Patients with $Sa\text{O}_2 < 90\%$	Patients with $Sa\text{O}_2 < 90\%$	Range of $Sa\text{O}_2$ in transit
I	52.4%	19%	74–100%
II	70.8%	20.8%	54–100%
III	55%	15%	83–99%
IV	64.3%	14.3%	80–100%
V	68.7%	34.4%	80–100%

technique used. There was, however, a trend towards a higher incidence of severe hypoxia in patients after upper abdominal surgery, although in the numbers studied this failed to achieve significance (and it was not thought reasonable to pursue the study to achieve such a result because of unacceptable degrees of desaturation during transit).

Postoperative hypoxia has been studied widely in the past but usually only single isolated measurements have been made (e.g. on days 1, 2 and 5) because this has required arterial blood gas analysis. However, McKenzie,[4] using multiple arterial sampling in the immediate postoperative period (0–10 minutes) following anaesthesia for repair of fractured neck of femur, demonstrated a very marked decrease in $Pa\text{O}_2$ in patients who breathed ambient air.

The recent introduction of pulse oximetry has made this type of study very much easier. The working principle of this equipment has been widely described[5,6] and the portability and noninvasive nature of the technique make it very useful for monitoring $Sa\text{O}_2$ in most clinical situations.[6,7]

Tyler *et al.*,[1] using pulse oximetry, noted a high incidence of desaturation following routine surgery in previously healthy patients during transit from theatre to the recovery area. They found no correlation with age or anaesthetic technique but did note a significant correlation between minimum $Sa\text{O}_2$ and patient weight (a variable not recorded in our study).

The overall incidences of hypoxia and severe hypoxia were lower in their study (35% and 12%) than in the present one (61.4% and 21.9%). This may be accounted for by the fact that the operations in their study were predominantly gynaecological.

Upper abdominal surgery is known to be associated with a high incidence of postoperative pulmonary complications. The main reasons advanced to account for this include a reduction in vital capacity, impaired coughing caused by pain[8] and diaphragmatic splinting which leads to a reduction in functional residual capacity. These factors may be responsible in part for the desaturation seen in the immediate postoperative period but other factors may also be involved.

Diffusion hypoxia produced by nitrous oxide elimination[9] may occur but this mechanism should be of fairly short duration (0–5 minutes). In the present study, 100% oxygen was administered at the end of anaesthesia and this should largely obviate diffusion hypoxia. Furthermore, the patients in our study who had not received nitrous oxide exhibited a similar degree of desaturation as those who had.

A low mixed venous saturation ($S\bar{v}\text{O}_2$) may also lead to arterial desaturation in patients who breathe air. An increase in oxygen demand as a result of postanaesthetic shivering, superimposed on a reduction in cardiac output produced by the residual effects of anaesthetic agents, has been suggested as a mechanism for the reduction in $S\bar{v}\text{O}_2$.[4]

Obesity is associated with an increase in V/Q maldistribution and this association was observed by Tyler.[1] In addition, incomplete antagonism of neuromuscular blockade may lead to hypoventilation, as may opioid-induced respiratory depression. With the exception of obesity, no other factor has yet been shown to predict the occurrence of significant desaturation in the immediate postoperative period.

In conclusion, we have confirmed that desaturation is a common and underdiagnosed problem in the immediate postoperative period. It appears to be more common after upper abdominal surgery, although it is not yet possible to predict which patients will become hypoxic. We recommend, therefore, that supplementary oxygen be given to *all* patients in the immediate postoperative period, including the period of transit from the operating theatre to recovery room in a large theatre complex. The duration of administration of oxygen to patients in the recovery room is a question that requires further investigation and debate.

References

1. Tyler IL, Tantisira B, Winter PM, Motoyama EK. Continuous monitoring of arterial oxygen saturation with pulse oximetry during transfer to the recovery room. *Anesthesia and Analgesia* 1985; **64:** 1108–12.
2. Marshall BE, Wyche MQ. Hypoxemia during and after anesthesia. *Anesthesiology* 1972; **37:** 178–209.
3. Vaughan RW, Engelhardt RD, Wise L. Postoperative hypoxemia in obese patients. *Annals of Surgery* 1974; **180:** 877–82.
4. McKenzie PJ. Anaesthesia for repair of fractured neck of femur. A comparison of spinal and general anaesthesia. MD Thesis, Oxford University, 1984.
5. Taylor MB, Whitwam JG. The current status of pulse oximetry. Clinical value of continuous non-invasive oxygen saturation monitoring. *Anaesthesia* 1986; **41:** 943–9.
6. Payne JP, Severinghaus JW, eds. *Pulse oximetry.* New York: Springer-Verlag, 1986.
7. Clapham MCC, Mackie AM. Pulse oximetry. An assessment in anaesthetised dental patients. *Anaesthesia* 1986; **41:** 1036–8.
8. Spence AA, Alexander JI. Mechanisms of postoperative hypoxaemia. *Proceedings of the Royal Society of Medicine* 1972; **65:** 12–14.
9. Fink BR. Diffusion anoxia. *Anesthesiology* 1955; **16:** 511–9.

Anaesthesia, 1987, Volume 42, pages 1316–1320

The use of opioids in neonates. A retrospective study of 933 cases

G. Purcell-Jones, BSc, MRCP, FFARCS, F. Dormon, MB, BS, FFARCS, Registrars, E. Sumner, BM, BCh, FFARCS, Consultant, Department of Anaesthesia, The Hospital for Sick Children, Great Ormond Street, London WC1 3JH.

Summary

This is a retrospective study on the use of postoperative opioids in neonates admitted to the surgical intensive care unit at Great Ormond Street over a 5-year period (1980–84). A total of 131 (14%) babies received opioids out of 933 neonates admitted to the unit. The use of opioids increased from 9.7% to 27.2% of admitted cases during the survey period. Postoperative ventilation of the lungs was necessary in 240 (25.7%) cases and 88 (36.6%) of these were given opioids. Four babies initially failed to wean from controlled ventilation as a result of opioid induced respiratory depression. A total of 51 (7.35%) spontaneously breathing neonates received opioids and seven (13.7%) of these developed apnoea or respiratory failure thought to be induced by opioids. The administration of opioids by nurses occurred most frequently in the late evening and early hours of the morning, when medical cover is at its lowest level.

Key words

Anaesthesia; paediatric.
Analgesia; opioids.

The limited physiological respiratory reserve of the neonate, combined with dependence on diaphragmatic breathing, leads to a high incidence of respiratory failure in this age group.[1] Pain after abdominal surgery may cause further limitation of respiratory mechanics which results in tachypnoea and reduced coughing.[1] Relief of such pain may improve respiratory function but the unpredictable neonatal sensitivity and pharmacokinetic response to opioids[2,3] have resulted in a reluctance to prescribe postoperative analgesia, in order to avoid respiratory depression.

Recently, however, metabolic, hormonal and neurophysiological responses to pain have been demonstrated in the newborn[4] and this has put pressure on the anaesthetist to prescribe postoperative analgesia.[5,6] Caution is traditionally advised with regard to the use of opioids in the neonate but much of the clinical evidence is anecdotal and the incidence of neonatal respiratory depression induced by opioids in this age group is unknown.

We have, therefore, reviewed the use of postoperative opioids and the associated incidence of respiratory depression in babies less than one month old admitted to the Surgical Intensive Care Unit at The Hospital for Sick Children, Great Ormond Street, London.

Method

The records of 933 neonates in the 5 years between 1 January 1980 and 31 December 1984 were reviewed. All underwent thoracic, abdominal or body surface procedures. Patients admitted for cardiac or neurosurgery are treated on separate intensive care units and were not included in this study. The use of opioids during intermittent positive pressure ventilation of the lungs (IPPV), continuous positive airway pressure (CPAP) and spontaneous ventilation in these patients was determined by cross-referencing the medical notes, nursing and controlled drugs records, and separate ventilation cards kept by the anaesthetists. The incidence of opioid use in the spontaneously breathing and ventilated neonate was thereby determined for each year of the survey.

The occurrence of opioid induced apnoea in the spontaneously breathing neonate was determined by exclusion. Apnoea was considered to be present when breathing ceased for longer than 30 seconds and active resuscitation was required to save the baby. The details of apnoea and resuscitation were recorded by anaesthetic or medical practitioners present at the resuscitation in all cases and confirmed in the nursing records. Those who developed apnoea in the presence

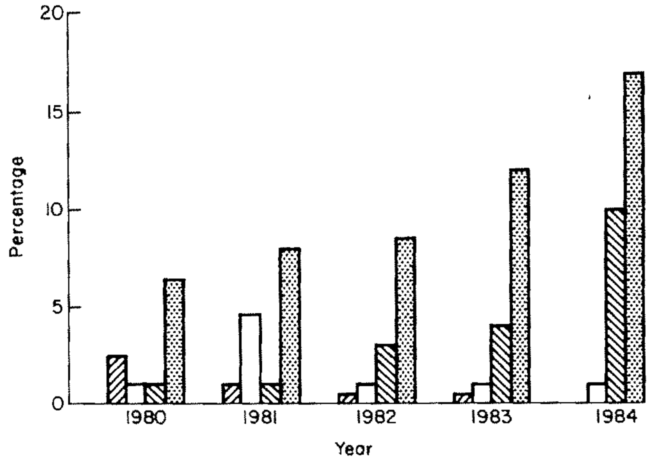


Fig. 1. Percentage of neonatal admissions who received opioids in the 5-year period 1980–84. ▨, Pethidine compound; □, papaveretum; ▧, codeine phosphate; ▩, morphine.

of a diagnosis of septicaemia, hypoglycaemia, hypocalcaemia, electrolyte disturbance or neurological disease were excluded. Opioids were accepted as the probable cause of apnoea only when given within 8 hours of the event and either naloxone or a period of supportive ventilation of the lungs was required to overcome the respiratory depression. Episodes of transient apnoea with spontaneous recovery were not included in this study.

Ventilation records were examined to ascertain the incidence of failure to wean from IPPV following opioid induced respiratory depression. A respiratory rate of less than 10 breaths/minute in the presence of normocarbia or hypercarbia, was presumed to indicate opioid induced respiratory depression when the opioid was prescribed within the 12 hours before the weaning attempt and no other sedatives had been prescribed. In addition, spontaneous recovery of respiratory drive following a short period of IPPV without further opioids and the absence of other causes of apnoea was required to confirm the diagnosis of opioid induced failure to wean.

Finally, the daily pattern of distribution of opioids administered by nurses was determined for the total number of doses given over the 5-year period.

Results

The use of opioid drugs in babies less than one month old increased noticeably over the 5-year period surveyed. These changes were largely accounted for by a dramatic increase in the use of morphine and codeine phosphate, whereas the use of papaveretum and injection pethidine compound BP (PethCo: pethidine 25 mg, promethazine 6.25 mg, chlorpromazine 6.25 mg in 1 ml) remained static (Fig. 1).

Ventilated patients. The total number of babies whose lungs were ventilated each year and the pattern of referral to the unit did not change significantly over the period surveyed. The most common indication for opioids was to coordinate ventilation in the presence of tachypnoea. Morphine sulphate was the most commonly prescribed opioid in ventilated babies. Of the babies who received this drug, 3.3% were already breathing unassisted and a further 7.7% were on CPAP. The use of different opioids in ventilated babies is shown in Table 1 and the number of babies whose lungs were ventilated, with and without opioids, is shown in Table 2.

Opioid induced failure to wean from IPPV occurred in four cases out of 88. These patients had received IPPV for one to three days after abdominal surgery between the 6th and 14th day of life and were prescribed morphine 0.1 mg/kg during ventilation. The number of doses given in the previous 12 hours varied from one to three. In each case no ventilatory drive was noted in the presence of normocarbia or hypercarbia, but this recovered following a further 12 hours of ventilation. They had not received any other form of sedation. No further respiratory problems occurred in these babies.

Spontaneously breathing patients. A total of 51 spontaneously breathing, unintubated neonates received postoperative opioids in some form; half (26) received intramuscular codeine phosphate. The latter drug was the most commonly used in spontaneously breathing babies. The number of neonates given opioids while breathing spontaneously increased over the period surveyed (Table 3). The use of individual opioids in spontaneously breathing babies is shown in Table 4. The incidence of respiratory depression and apnoea in this group was 13.5%; five cases suffered

Table 1. Numbers of neonates who received opioids during IPPV per year.

Opioid	Dose (mg/kg)	1980	1981	1982	1983	1984	Totals
Morphine	0.1	13	11	15	15	29	83
Codeine phosphate	1.0	0	0	0	1	1	2
Papaveretum	0.25	0	3	0	0	0	3
Totals		13	14	15	16	30	88

Table 2. Number of admissions and treatment during IPPV in surgical ITU.

	1980	1981	1982	1983	1984	Totals
Total admissions	194	180	186	193	180	933
Number who received IPPV	47	42	50	50	51	240
(% admissions)	(24.2)	(23.3)	(26.8)	(25.9)	(28.3)	(25.7)
Number who received opioids during IPPV	13	13	15	16	31	88
(% of those who received IPPV)	(27.6)	(30.9)	(30.0)	(32.0)	(60.7)	(36.6)

Table 3. Numbers of patients who breathed spontaneously and received opioids and who developed respiratory complications.

	1980	1981	1982	1983	1984	Totals
Total breathing spontaneously	147	138	136	143	129	693
(% admissions)	(76.8)	(77.7)	(74.2)	(74.1)	(71.1)	(74.3)
Total prescribed opioids	19	15	20	28	49	131
(% admissions)	(9.7)	(8.3)	(10.7)	(14.5)	(27.2)	(14.0)
Number with complications	9	4	8	11	19	51
(% admissions)	(4.6)	(2.2)	(4.3)	(5.7)	(10.5)	(5.5)

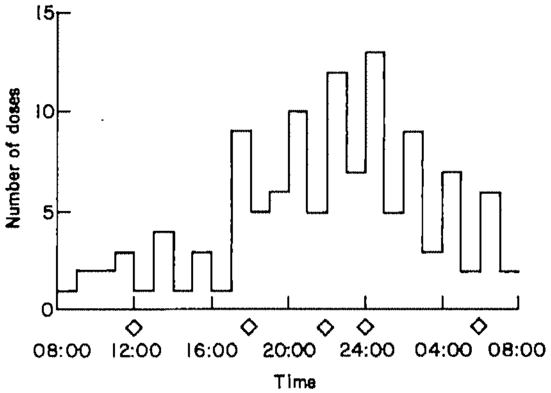


Fig. 2. Opioid administration pattern in spontaneously breathing neonates according to time of day (diamonds indicate normal drug rounds.)

from apnoea and two cases developed marked respiratory depression. None of these seven cases received any sedatives other than opioids. Three followed appropriate doses of papaveretum, two followed PethCo and two followed codeine phosphate. All the patients recovered after appropriate resuscitative efforts including stimulation, oxygen, bag and mask manual ventilation, tracheal intubation and naloxone. Six of the seven patients had abdominal surgery. Figure 2 shows the use of opioids in relation to the time of day. All the cases of apnoea occurred during the period 22:30 hours to 07:45 hours.

Discussion

An acceptance that neonatal pain requires treatment is reflected in the increasing use of opioids that we have demonstrated in both ventilated and unventilated babies. Unfortunately, this practice has been associ-

Table 4. Numbers of spontaneously breathing and ventilated neonates who received different opioids, and associated respiratory complications.

Opioid	Dose	Total prescribed opioids	Spontaneous ventilation	Respiratory depression	IPPV	Failure to wean
Morphine	0.1 mg/kg	89*	10	0	83	4
Papaveretum	0.25 mg/kg	11	8	3	3	0
Codeine phosphate	1.0 mg/kg	28	26	2	2	0
Pethidine compound	0.05 ml/kg	8	8	2	0	0
Totals		136†	52§	7	88	4

* Four children received morphine both while they were ventilated and while they breathed spontaneously.

† Five children received two different opioids.

§ One child received two different opioids.

ated with an increasing number of respiratory complications. The potential risks of using opioids are reduced in ventilated babies by the fact that all are intubated and nursing observation is consequently greater and a reduction in respiratory drive can be treated rapidly with simple adjustments to the ventilator. This was the case in the small number who failed to wean in this study. The difficulties that they encountered would have been avoided by delaying the weaning attempt for 12 hours after the last opioid administration. The use of opioids in such controlled circumstances should probably be encouraged.

In contrast, apnoea in the spontaneously breathing neonate is potentially catastrophic and the means for immediate intubation must be available. The administration of bolus doses of opioids in spontaneously breathing neonates produced a 13.5% incidence of respiratory depression, all of which occurred in the sleeping hours. The increased administration of opioids in the night and early hours of the morning is consequently worrying and the reasons for it are not immediately apparent. The high incidence of respiratory arrest following papaveretum (three out of eight cases) may be a reflection on the dose, which was larger than the dose of 0.15 mg/kg now recommended by Roche.[7] However, at that time no dose recommendations were available and the papaveretum data sheet dose (0.15 mg/kg) is still not supported by any published data. Papaveretum and injection PethCo are no longer used in surgical neonates at this hospital. Morphine sulphate (0.1 mg/kg) and codeine phosphate (1 mg/kg) seem to be safer choices in neonates breathing spontaneously, since only two out of 28 babies who received codeine and none out of 10 who received morphine developed respiratory depression. A single dose of codeine phosphate (1 mg/kg) has not induced respiratory failure in our experience and has provided good analgesia. However, the use of this drug in newborns and neonates by specialist paediatric anaesthetists is very limited (Dormon, Purcell-Jones and Sumner, unpublished observations).

The majority of neonates in this study (86%) did not receive any form of analgesia because there was no objective evidence that it was required. However, many of those ventilated without opioids received other forms of sedation, such as chloral hydrate. The traditional reluctance of anaesthetists to prescribe opioid analgesia to a postoperative neonate has been challenged by workers in the field of pain research and psychology.[5,6] Most agree that pain occurs but are unsure of its extent and whether the neonatal ability to detect nociceptive stimuli is fully developed. Exact indications for analgesia in the neonates we studied had rarely been recorded and evidence that the baby was in pain and required analgesia was usually a high pulse and respiration rate, supported by an overall impression of distress. In order to treat pain one needs to know the degree of pain present and then prescribe an appropriate choice and strength of analgesic agent to combat it. However, insufficient information is available for this practice in neonates. Quantification of neonatal pain could result in a measured prescribing response. Unfortunately, such quantification is almost nonexistent and our understanding of neonatal pharmacokinetics is equally limited. The only drug studied to data in spontaneously breathing neonates has been morphine,[1] although alfentanil[8] has been studied in ventilated babies. The limited knowledge available[1,2,3,8] indicates that the unpredictable neonatal response to opioids is the result of their altered pharmacokinetic handling and increased sensitivity. The latter is related to the immature blood–brain barrier and glucuronide metabolism in this age group. All these factors result in a narrow therapeutic range and the use of bolus doses must therefore be questioned. The use of opioid infusions would appear to be a more logical means to maintain minimum central levels for analgesia and thereby avoid respiratory depression. Duncan[1] has suggested that a morphine infusion regimen of 10 μg/kg/hour in unventilated neonates will not cause apnoea.

Neonates undoubtedly feel pain and may require analgesia. The administration of analgesia carries an obvious risk and opioids should not be prescribed unless appropriate facilities for immediate resuscitation are available. Thus, there is a need for controlled prospective comparative studies of the use of opioids in neonates so that firm guidelines can be provided for their safe use.

Acknowledgments

We would like to thank L. Connor and J. Stubbs for their help in the preparation of the manuscript.

References

1. Duncan A. The postoperative period. *Clinics in Anaesthesiology* 1985; **3:** 619–32.
2. Way WL, Costley EC, Leong Way E. Respiratory sensitivity of the newborn infant to meperidine and morphine. *Clinical Pharmacology and Therapeutics* 1965; **6:** 454–61.
3. Brown AK, Zwelzer WW, Burnett HH. Studies on the neonatal development of the glucuronide conjugation system. *Journal of Clinical Investigation* 1958; **37:** 332–40.
4. Anand KJS, Brown MJ, Causon RC, Christofides ND, Bloom SR, Aynsley-Green A. Can the human neonate mount an endocrine and metabolic response to surgery? *Journal of Pediatric Surgery* 1985; **20:** 41–8.
5. Owens ME. Pain in infancy: conceptual and methodological issues. *Pain* 1984; **20:** 213–30.
6. Richards T. Can a fetus feel pain? (Editorial). *British Medical Journal* 1985; **291:** 1220–1.
7. *ABPI data sheet compendium 1986–87.* Datapharm Publications Ltd/London: Omnopon Paediatric Ampoules, 1986: 1309–10.
8. Meistelman C, Levron JC, St Maurice C, Gerbaut L. Plasma protein binding of alfentanyl in newborns, infants and children. *First European Congress of Paediatric Anaesthesia, Rotterdam, August 1986* (Abstract).

Anaesthesia, 1987, Volume 42, pages 1320–1323

Comparison of trichloroethylene and enflurane as adjuncts to nitrous oxide and relaxant anaesthesia

A. S. C. Rice, MB, BS, Registrar, F. Reynolds, MD, FFARCS, Department of Anaesthetics, St Thomas' Hospital, London SE1 7EH.

Summary

Forty women who underwent gynaecological surgery were randomly allocated to receive trichloroethylene, enflurane, or enflurane plus fentanyl as adjuncts to nitrous oxide/relaxant anaesthesia with controlled ventilation. No serious cardiac dysrhythmias were seen in any group. Each patient was observed postoperatively for 4 hours by a nurse blind to the technique used, and questioned at 24 hours by a similarly blinded anaesthetist. Recovery after trichloroethylene was not significantly prolonged although postoperative analgesia by visual analogue was better, opiate analgesia was required less frequently and there was less nausea and vomiting than in either of the enflurane groups.

We argue for the continued use of trichloroethylene by this technique, because it costs one hundred times less than enflurane and because of the potential morbidity of the postoperative opiate dosage required after enflurane.

Key words

Anaesthetics, volatile; enflurane, trichloroethylene.
Complications; postoperative.

Trichloroethylene has been little used since the advent of more modern inhalational agents such as halothane and enflurane. It developed a reputation for causing dysrhythmias,[1] tachypnoea and postoperative nausea, vomiting[2,3] and sedation when used in patients who breathed spontaneously, in whom unmonitored and often high concentrations were administered.[4] It is, however, a potent analgesic and might therefore produce postoperative pain relief.

The cost of trichloroethylene compared to other agents is also in its favour in the current climate.[5] The cost per hour at a fresh gas flow of 8 litres/minute is:[6] 1% enflurane, £3.25; 0.5% halothane, £0.47; 0.5% trichloroethylene, £0.04. The Manley ventilator, which requires a high fresh gas flow, is in routine use in this hospital. Since halothane anaesthesia may be used for preliminary diagnostic procedures, we compared trichloroethylene with enflurane as an adjunct to nitrous oxide and relaxant anaesthesia for gynaecological laparotomy.

Methods

Selection of patients. Forty women otherwise in good health (ASA grade 1 or 2) were selected and were to undergo gynaecological surgery that involved lower abdominal laparotomy (Wertheim's hysterectomy was excluded). They were visited the evening before sur-

---

Correspondence should be addressed to Dr F. Reynolds please.

gery, verbal consent was obtained and the questions which they would be required to answer postoperatively were explained. They were not aware to which group they would be assigned.

Anaesthesia. All patients were premedicated with papaveretum 10–20 mg and hyoscine 0.2–0.4 mg intramuscularly 1–2 hours pre-operatively. Anaesthesia was induced with thiopentone and alcuronium 0.25 mg/kg. After tracheal intubation patients were ventilated with nitrous oxide 5.5 litres/minute and oxygen 2.5 litres/minute. They were randomly allocated to receive either enflurane 1%, enflurane 1% with fentanyl 1–2 μg/kg, or trichloroethylene 0.5% initially; the inspired concentration was adjusted according to the patient's response. The electrocardiogram and arterial blood pressure were monitored. Trichloroethylene was stopped as the peritoneum was closed, and enflurane as the subcutaneous layer was stitched. Residual neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrronium 0.6 mg.

Recovery. The patients were assessed for 4 hours in the theatre recovery area by an experienced nurse who did not know which volatile agent the patient had received. She was instructed to assess the patient's pain on waking, using a 10-cm visual analogue scoring system (VAS), to give analgesic and antiemetic drugs as she felt they were required and to note the time at which she would have judged the patient fit to return to the ward. At the end of each hour she recorded the presence of nausea, vomiting, distress, disorientation or shivering.

Postoperative visit. Within 24 hours of the patient's return to the ward she was visited by one of the authors who did not know which volatile anaesthetic she had received. The following were recorded: the patient's assessment of pain on waking, using the VAS; whether she felt sick or vomited during recovery; and the total dose of analgesics and antiemetics in the first 4 postoperative hours.

Statistical analysis. The Chi-squared test was used to compare numerical data. Pain scores and analgesic doses were compared using unpaired *t*-tests. The mean heart rate and systolic arterial blood pressure were calculated for individual patients from the available intra-operative readings and the mean of the means and the standard deviation calculated for each treatment group. Because operations varied in length it was appropriate to assess circulatory stability not from individual standard deviations but rather, from individual maximum ranges.

Results

There were no significant differences in age, weight, thiopentone dose, type of incision or duration of surgery between the three groups (Table 1).

Circulatory changes. During surgery the average mean heart rate with enflurane alone was slightly higher and the systolic arterial blood pressure slightly lower than in the other two groups, although the differences were not significant. Maximum ranges did not differ between the groups (Table 2). Dysrhythmias were not troublesome in any group (Table 3).

Table 1. Clinical data. Values expressed as mean (SD).

	Trichloroethylene ($n = 14$)	Enflurane ($n = 13$)	Enflurane + fentanyl ($n = 13$)
Age, years	37.4 (8.5)	43.7 (9.4)	38.0 (8.0)
Weight, kg	65.5 (9.5)	65.0 (12.1)	60.4 (11.5)
Dose of thiopentone, mg/kg	6.2 (1.0)	5.7 (1.8)	5.9 (1.3)
Incision			
Pfannenstiel	13	12	11
Lower mid-line	1	1	2
Duration of surgery, minutes	66.8 (34.3)	63.8 (21.1)	75.0 (28.1)

Table 2. Intra-operative circulatory changes. Values expressed as mean (SD).

	Trichloroethylene	Enflurane	Enflurane + fentanyl
Mean heart rate, beats/minute	74.5 (7.0)	83.5 (18.1)	75.5 (23.3)
Maximum range	22.1 (11.6)	23.1 (10.7)	23.9 (23.3)
Mean systolic blood pressure, mm Hg	114.9 (12.0)	109.8 (12.4)	115.2 (16.3)
Maximum range	26.1 (12.6)	31.6 (15.2)	37.7 (17.3)

Table 3. Peri-operative dysrhythmias.

Group	Dysrhythmia
Trichloroethylene	Short period first degree heart block (<5 minutes) Short period nodal rhythm (<5 minutes)
Enflurane	Persistent sinus tachycardia × 1 Sinus tachycardia × 2 Sinus bradycardia × 1
Enflurane + fentanyl	Sinus tachycardia × 2

In two of the patients who received enflurane alone, signs of stress during the course of the operation were such that it was judged unethical to withhold fentanyl. These two were therefore included in the enflurane plus fentanyl group for the assessment of *postoperative* changes.

Postoperative pain and recovery (Table 4). There was no significant difference in recovery time between the three groups. The pain score on recovery as judged by the nurse was significantly less with trichloroethylene than with enflurane plus fentanyl or the combined enflurane groups. The patients also recorded pain as least with trichloroethylene but the difference was not significant. However, 50% of the trichloroethylene patients required no analgesia at all during the first 4 postoperative hours, and three of these required no analgesia throughout the first 24 hours. Despite apparently good recovery from anaesthesia, the dose of papaveretum during the first 4 hours was signifi-

Table 4. Postoperative pain and recovery. Values expressed as mean (SD).

	Trichloro-ethylene	Enflurane	Enflurane + fentanyl
Recovery time, minutes	56 (24)	39 (21)	65 (59)
Pain score (VAS) on recovery, cm			
Nurse*	2.86 (3.03)	4.35 (2.16)	5.54 (2.31)
Patient	3.23 (3.36)	5.56 (3.38)	4.98 (3.16)
Analgesia requirement in first 4 hours			
Number of patients	7 (50%)	13 (100%)	13 (100%)
Dose of papaveretum,† mg	8.21 (8.68)	15.7 (6.41)	18.5 (9.22)

* Trichloroethylene versus enflurane + fentanyl, $p < 0.02$; trichloroethylene versus combined enflurane group, $p < 0.05$.
† Trichloroethylene versus enflurane, $p < 0.01$; trichloroethylene versus enflurane + fentanyl, $p < 0.02$.

Table 5. Frequency of side effects in first 4 postoperative hours.

	Trichloroethylene ($n = 14$)	Enflurane ($n = 11$)*	Enflurane + fentanyl ($n = 15$)*
Nausea			
Nurse	4	5	6
Patient	2	4	3
Disorientation and/or distress	6	5	7
Shivering	3	3	4

* In fact, neither patient who was transferred from the enflurane to the enflurane plus fentanyl group experienced any postoperative side effects, so the results were unaffected.

cantly less following trichloroethylene than in the enflurane groups.

Postoperative side effects (Table 5). No patient vomited during the first 4 postoperative hours, and no patient vomited at all following trichloroethylene although three did in the enflurane groups. There was less nausea following trichloroethylene than following enflurane, with or without fentanyl, although the difference was not significant. There was no difference in the frequency of distress, disorientation or shivering between the groups.

Discussion

Trichloroethylene was introduced into anaesthetic practice in 1941,[7] before the days of temperature-compensated, calibrated vaporizers and of the widespread use of neuromuscular blockade. Rapid shallow respiration must often have led to hypercarbia and hypoxia which, coupled with the use of inhaled concentrations of anything up to 10 MAC, led to cardiac dysrhythmias in about two-thirds of patients.[4] Wide use of controlled ventilation using the circle absorber, and then of halothane, dramatically curtailed its use. Now that the circle absorber has declined in use in favour of high flow, non-return systems such as the Bain, and the Manley ventilator for controlled ventilation, and repeat halothane anaesthetics are unadvisable,[8] there is a need for a low cost volatile agent.

In the present study, trichloroethylene was no less satisfactory intra-operatively than enflurane as an adjunct to the nitrous oxide and relaxant technique. Circulatory stability was good and opioid analgesia was never required. Dysrhythmias were not a problem. With the use of an accurate modern vaporizer such as the Tritec 3, of lower concentrations of trichloroethylene than are necessary to maintain anaesthesia in an unparalysed patient, and with controlled ventilation, dysrhythmias are not a prominent feature.[4] Moreover, although tachypnoea was sometimes observed briefly on reversal of neuromuscular blockade, it appeared merely to promote an easy return of spontaneous respiration.

Another objection to trichloroethylene has been that its high blood/gas partition coefficient renders it slow to act[9] and cumulative. A slow onset is easily overcome by administration of an initial loading concentration of 0.5%, that is, in excess of MAC. Trichloroethylene, which is a halogenated hydrocarbon rather than a halogenated ether, is nonirritant and therefore a loading dose can readily be given, while residual effect is manifest as postoperative analgesia. Moreover, Davidson[4] pointed out its value when used in low concentration during controlled ventilation as an inhalational narcotic, when it produces analgesia without the danger of postoperative respiratory depression inherent in the use of opioids.

Recovery was apparently not delayed following trichloroethylene in this study, according to the recovery room nurse's routine assessment, but the analgesic effect in the postoperative period was striking. Both nurse and patient assessed pain on recovery as least in the trichloroethylene group, although the difference between the groups in the patients' assessment was not significant. The patients' retrospective assessment probably included the period following administration of papaveretum in some cases. The prolonged analgesia following trichloroethylene was also reflected in the markedly reduced requirement for systemic opiates in the postoperative period.

Trichloroethylene, despite its reputation,[2,3,10] produced slightly though not significantly less nausea than enflurane, with or without fentanyl. Opioids are probably the most potent emetics used in this context; therefore, nausea beyond the first 4 postoperative hours was not quantified in this study. The use of trichloroethylene, however, must reduce the incidence of morbidity associated with opioids. Other side effects were infrequent in the postoperative period in all groups. Liver function tests were not performed but no jaundice or other serious anaesthetic sequelae, such as cranial nerve palsy, were observed.

Conclusion

This study suggests that trichloroethylene, when used in a suitable inspired concentration during controlled ventilation, produces good operative conditions and a stable circulation, while postoperative analgesia is impressive and side effects few. It therefore compares favourably with enflurane and is also one hundred times cheaper.

Acknowledgments

We thank the recovery room nurses for their unfailing willingness to help.

References

1. Barnes CG, Ives J. Electrocardiographic changes during Trilene anesthesia. *Proceedings of the Royal Society of Medicine* 1944; **37**: 528–32.
2. Wood M. Inhalational anaesthetic agents. In: Wood M, Wood A, eds. *Drugs and anesthesia*. Baltimore: Williams and Wilkins, 1982: 270.
3. Vickers MD, Schneider M, Wood-Smith FG. *Drugs in anaesthetic practice*, 6th edn. London: Butterworths, 1984: 140.
4. Davidson JT. Trichloroethylene: a plea. *Anaesthesia* 1984; **39**: 501–2.
5. Lethbridge JR, Secker Walker J. Cost of anaesthetic drugs and clinical budgeting. *British Medical Journal* 1986; **293**: 1587–8.
6. Reynolds F. Trichloroethylene. *Anaesthesia* 1984; **39**: 932.
7. Hewer CL, Hadfield CH. Trichloroethylene as an inhalation anaesthetic. *British Medical Journal* 1941; **1**: 924–7.
8. Pembleton WE. Trichloroethylene anesthesia reevaluated. *Anesthesia and Analgesia* 1974; **53**: 730–3.
9. Wylie D, Churchill-Davidson HC, eds. *A practice of anaesthesia*, 5th edn. London: Lloyd Luke, 1984.
10. Farman JV. Some long established agents—a contemporary review. *British Journal of Anaesthesia* 1981; **53**: 3S–9S.

Anaesthesia, 1987, Volume 42, pages 1323–1326

Protocols in obstetric units: their use in Wales in 1983*

B. Owen, BSc, MB, BCh, FFARCS, Consultant, Ysbyty Glan Clwyd, Bodelwyddan, Clwyd LL18 5UJ, Wales.

Summary

The Welsh Perinatal Mortality Initiative carried out an extensive enquiry into perinatal deaths in Wales between 1984 and 1986 and their report was published by the Secretary of State for Wales in December 1986. One aspect examined was the obstetric anaesthetic service and a comprehensive questionnaire was sent to all obstetric units where Caesarean sections are carried out. One of the questions was on the use of protocols in obstetrics and the results presented are disappointing.

Key words

Anaesthesia; obstetric.

The third report from the Social Services Committee on Perinatal and Neonatal Mortality[1] in the 1983–84 session recommended that the DHSS and the profession examine ways to ensure the provision of a safe obstetric anaesthetic service throughout the country. In the second report of the Maternity Services Advisory Committee[2] to the Secretaries of State for Social Services and for Wales, the Chairman, Dame A. Munro, wrote in her foreword 'We found organisational weaknesses in the service. Much more needs to be done within hospitals to develop agreed written operational policies which are clearly defined and are understood by all professionals concerned. Without these, confusion over who does what and when can and does result.'

One of the questions in a questionnaire circulated by the Welsh Perinatal Mortality Initiative Survey Group[3] in 1984 to assess obstetric anaesthetic services was on the use of protocols in obstetric units where Caesarean sections are carried out regularly.

Method

Twenty units where an anaesthetic service is provided regularly for Caesarean sections were circulated with a questionnaire and an explanatory letter. Nineteen of these units were consultant obstetric units and one an isolated general practitioner obstetric unit. A copy of the questionnaire was sent to one consultant anaesthetist with a known interest in obstetric anaesthesia by the author, and to one consultant obstetrician by Professor B. Hibbard (Member of the Initiative Group) in all consultant units. They were asked to liaise in completion of the questionnaire and to return one copy to the author. The questionnaire was completed by a general practitioner anaesthetist who is a Fellow of the Faculty of Anaesthetists in one unit.

---

* Based on a paper given at the Association of Anaesthetists' Annual Meeting in London, September 1986.

The question asked was, do you have agreed protocols on the following: antacid therapy; the use of H_2-receptor antagonists; severe haemorrhage; cardiac arrest; failed intubation; epidural analgesia; dural tap; unexpected total spinal. If the answer was affirmative they were asked to send copies of the protocols when they returned the questionnaires.

A score of 1 was given for each protocol in the unit. The best units would therefore have a protocol for each item and a maximum score of 8. The author visited all units to check the results after the questionnaires were returned.

Results

There was great variation in the number of protocols found in the units, as seen in Figs 1 and 2 which give an overall view for 1984, and in Table 1. A protocol for antacid therapy was found in 18 units originally but all units had a policy when the visit was made. Seventeen units used sodium citrate and three, magnesium trisilicate. H_2-receptor antagonists were used pre-operatively in eight units. A protocol for dealing with catastrophic haemorrhage was found in 10 units. Twelve units had a written protocol for cardiac arrest although 13 hospitals had a cardiac arrest team. Instruction to staff on the procedure to be followed if a cardiac arrest occurred, was given at intervals from 6-monthly to infrequently. In 12 units, where 55% of births in Wales took place, no regular instruction was given to midwives on the procedure to be followed should a cardiac arrest occur. A protocol for failed intubation was found in nine units.

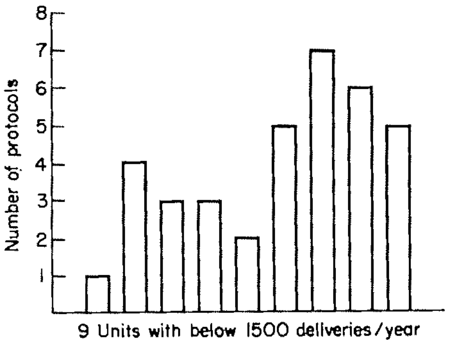


Fig. 1. Nine units with below 1500 deliveries/year: number of protocols/unit.

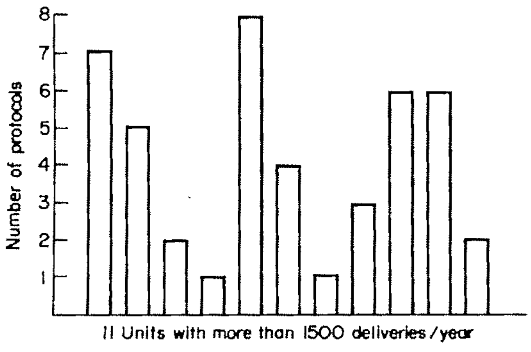


Fig. 2. Eleven units with more than 1500 deliveries/year: number of protocols/unit.

Table 1. Protocols found in 20 obstetric units.

Protocol	Number of units
Use of antacids	18
Use of H_2-receptor antagonists	8
Severe haemorrhage	10
Cardiac arrest	12
Failed intubation	9
Epidural analgesia	8
Dural tap	8
Unexpected total spinal	8

Protocols for epidural analgesia, dural tap and unexpected total spinal were found in the same eight units. Six of these units used epidural analgesia for labour and Caesarean sections, one for Caesarean section and one for labour for very few mothers. Eight units which used this technique did not have protocols. When all the units were examined, six had six to eight protocols; four of these had over 1500 deliveries/year and two below 1500 deliveries/year. Eight units had three to five protocols; three of these had over 1500 deliveries per year and five below this. Six units had only one or two protocols; four had over 1500 deliveries/year and two below. When protocols for antacid therapy, difficult/failed intubation and severe haemorrhage are looked at, only four units had these three protocols and 17% of the total 33 000 births in the survey took place in these units.

Discussion

The question asked was on the availability of eight protocols in a unit. This is not a comprehensive list one would expect to find in a well run obstetric unit but was used to provide an indication of the consultant anaesthetists' input into that unit.

In the *Report on Confidential Enquiries into Maternal Deaths 1979–81*,[4] 22 deaths were directly attributable to anaesthesia and anaesthesia was a contributing factor in a further seven deaths. The anaesthetic procedure was most commonly given for an emergency Caesarean section and it is at this time that anaesthetists in training usually work when they are not under the direct supervision of the consultant. Written guidelines which are agreed by all staff who work in the obstetric unit should ensure that newcomers to the unit are aware of the policies laid down if these are presented when they take up their appointment. Such guidelines should be regarded not as a replacement for teaching but as an adjunct or *aide memoire* readily available for consultation if there is uncertainty as to a unit's policy. The results indicate that some units need to update their policies and that others need to provide a comprehensive range of protocols.

Sweeney and Wright[5] found that despite its limitations, magnesium trisilicate remains the most popular antacid during labour and before Caesarean sections. The results presented show that it is used in only three units in Wales. Five mothers in the 1979–81 *Confidential Enquiries into Maternal Deaths*[4] died from aspiration pneumonitis and all had received magnesium trisilicate. Reynolds[6] has pointed out the potential danger and apparent ineffectiveness of this particulate, bulky and slow-acting antacid and the *Confidential Enquiries*[4] state that the inhalation of magnesium trisilicate is as harmful to the lungs as the inhalation of normal stomach contents.

Aspiration pneumonitis might disappear with the use of H_2-receptor antagonists which reduce volume as well as acidity, and of quick-acting nonparticulate antacids such as sodium citrate which need not be given prophylactically. These policies could be introduced for little cost.[7] Seventeen units used sodium citrate and only eight of these also used an H_2-receptor antagonist to reduce the volume of stomach contents.

The *Confidential Enquiries*[4] state that no food or fluids should be given by mouth during labour and that consideration should be given to emptying the stomach with an oesophageal tube before anaesthesia, particularly when large doses of narcotics have been given. Units should consider written guidelines on this. Again, the *Report*[4] draws the attention of obstetricians and anaesthetists to the necessity for a drill for the management of severe haemorrhage but in only half the units in Wales was this provided. The *Report* recommends that the drill must include provision of extra staff in emergency, the ready supply of blood and, above all, staff properly experienced in the management and monitoring of patients who are bleeding. It includes suggested guidelines for the management of major obstetric haemorrhage and points out that anaesthetists should be alerted when patients are admitted with antepartum haemorrhage.

Hanson[8] pointed out that a cardiac arrest is rare in obstetric practice and, for this reason, staff must be trained to recognise and deal with an arrest efficiently and effectively. Gaylard and Wilson[9] suggested that instruction in resuscitation techniques for obstetric medical staff in particular is essential if occasional disasters are to be avoided. Twelve units had a written protocol for cardiac arrest but practical instruction to staff on procedures to be carried out was haphazard and 12 units gave no instruction to midwives. Teamwork is essential when cardiac arrest occurs and all staff who work in the unit should have regular instruction on what to do, as well as written instruction to which they can refer.

Nine units had a protocol for failed intubation. The *Confidential Enquiries*[4] included eight mothers who died due to difficulty with intubation. In four mothers the tube was placed in the oesophagus. Four of the deaths were due to persistence with intubation. It was pointed out that there appeared to be no awareness of the risks from anoxia and from inhalation of stomach contents, or of the strong possibility of oesophageal intubation in difficult cases in this series; there was no drill for its management in the hospitals concerned.

Protocols for epidural analgesia in labour and for Caesarean section, as well as for complications which can follow the use of this technique, should be available in all units where it is carried out so that guidelines are provided for the safety of mother and fetus. Of 16 units that offered this service, however, only eight had protocols.

The results show that the number of protocols in the units does not depend on the number of deliveries in the unit. The paucity of protocols is more worrying the larger the unit because of the greater number of mothers involved and the likelihood that staff in training may provide anaesthesia for emergency procedures.

Conclusion

These results are disappointing, since the 1976–78 *Confidential Enquiries into Maternal Deaths*[10] had previously recommended drills for units. Anaesthetists do not receive copies of the *Confidential Enquiries into Maternal Deaths* but all those involved in obstetric anaesthesia should ask for copies from their Health Authorities in order that they can act on the recommendations made.

Protocols are cheap to produce, they ensure greater safety for the mother and greater awareness of problems and their treatment by all staff who work in the obstetric unit, so that when an emergency arises there can be a team approach. They should be readily available for all to read, preferably in a ring binder form so that the individual protocols can be updated with advancement in knowledge, or change of site of the unit. They should be agreed policy by the anaesthetic and obstetric divisions. Maternity service liaison committees should ensure that there are adequate protocols in all obstetric units in their districts.

Acknowledgments

The author thanks Professor B. Hibbard, Member of the Perinatal Mortality Initiative Survey Group, all the consultant anaesthetists and obstetricians in Wales who completed the questionnaire, T. Bailey, Medical

Anaesthesia, 1987, Volume 42, pages 1327–1339

Correspondence

Delayed convulsions after day case anaesthesia with enflurane 1327
L.T. Fahy, FFARCS
Analgesia for neonates 1328
I.S. Gauntlett, FFARCS
Preferential oxygen leak—an unusual case 1329
C.D. Hanning, FFARCS, D. Kruchek, MB, BS and A. Chunara
P. Sim 1330
Gross hypernatraemia associated with the use of antiseptic surgical packs 1331
C.C. Wise, FFARCS
J.M. Thorp, MRCP, FFARCS, I. MacKenzie, FRCS and E. Simpson, MCB, MRSC 1331
Ventolin nebules 1332
D.S. Mackie, FFARCS
Intratracheal pressure during controlled ventilation in infants 1332
G.B. Drummond, FFARCS
A. Synnott, FFARCSI, W.S. Wren, FFARCS and J. Davenport 1333
Auto-antagonism of buprenorphine 1334
F. Reynolds, MD, FFARCS
Unstable cervical fracture 1334
N. Braude, FFARCS
J.R. Eason, FFARCS, C.N. Swaine, FFARCS and P.I.E. Jones, FFARCS 1334
A new ventilator for closed breathing systems 1335
M.F.M. James
J.L. Plenderleith, FFARCS 1335
A. Twigley, FFARCS, M.K. Chakrabarti, BSc and J.G. Whitwam, PhD, FRCP, FFARCS 1335
Air–oxygen mixtures 1336
D.C. White, FFARCS
H. Moseley, FFARCS, A.Y. Kumar, MD, K.B. Shankar, MD and P.S. Rao, PhD 1336
Reservoir volume in a drawover system 1337
S. Yoganathan, FFARCS, RAMC, I.G. Johnston, FFARCSI, RAMC and I.T. Houghton, FFARCS, RAMC
A. Mackie, FFARCS 1337
Oesophageal stethoscope 1337
J. O'Dea, FFARCSI and I. Hall, FFARCS
Arterial to end tidal carbon dioxide tension difference during anaesthesia for tubal ligation 1338
G.D. Puri, MD
K.B. Shankar, MD, H. Moseley, FFARCS, Y. Kumar, MD, V. Vemula, DA and A. Krishnan, DA 1338
Intravenous injections 1339
I.E. Tweedie, MB, ChB

Delayed convulsions after day case anaesthesia with enflurane

The occurrence of delayed convulsions in non-epileptic patients after enflurane anaesthesia has important implications for the increased use of this agent in day case anaesthesia, as illustrated by the following case.

A healthy, 30-year-old man presented for vasectomy under general anaesthesia. He had a grand mal seizure 9 years earlier after an intramuscular injection of lignocaine but there was no previous history of idiopathic epilepsy. He had not had a convulsion since that episode and had received two uneventful general anaesthetics for minor orthopaedic procedures.

Anaesthesia was induced with thiopentone 400 mg and maintained with nitrous oxide 66% in oxygen and enflurane 1–5%, with spontaneous ventilation via a Magill system. Fentanyl was given intravenously in increments during the procedure to a total of 100 μg. Duration of anaesthesia was 25 minutes; the patient

---

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

made an uneventful recovery and was discharged 5 hours postoperatively. He had what appeared to be a classical grand mal seizure en route home, as a passenger in a car driven by his wife, with loss of consciousness for approximately 10 minutes. He was re-admitted for overnight observation and was fully conscious with no residual neurological signs.

The tendency of enflurane to lower the seizure threshold in previously non-epileptic patients may manifest itself over an entire spectrum from electroencephalographic changes with myoclonic activity,[1] to grand mal seizures.[2] Convulsions may occur with or without loss of consciousness[3] at any time from the recovery phase[3] up to 8 days postoperatively.[2]

The change of anaesthetic practice away from the use of halothane is apparent and enflurane has been advocated as a preferable volatile agent especially for day case anaesthesia, where expeditious recovery is desirable. However, the incidence of halothane hepatitis on which this development is based, is acknowledged to be low. The risk of precipitation of a grand mal seizure with enflurane must be put against this risk. Patients are usually advised to avoid activities such as driving, operating machinery and drinking alcohol within 24 hours of general anaesthesia, so the consequences of seizures induced by enflurane which may occur within this period, as with our patient, should thus be mitigated. However, their later occurrence raises the question of whether the period of this prohibition should be extended accordingly if enflurane is used and whether anaesthetists are at legal peril if they neglect to give this advice.

The risk of grand mal seizures after enflurane anaesthesia has not been completely assessed. Spence[4] commented on the movement away from halothane and put the point succinctly: 'On the grounds of toxicity, such a shift in practice is without real foundation for it could only be after large scale comparisons of these compounds, of a type which has not been undertaken, that the relative merits of each could be agreed.'

Arrowe Park Hospital,
Wirral,
Merseyside L49 5PE

L.T. Fahy

References

1. Bostem F, Hanquet M, Gallez JP. Enflurane (Ethrane) and EEG. *Acta Anaesthesiologica Belgica* 1974; **25:** 233–45.
2. Ohm WW, Cullen BF, Amory DW, Kennedy RD. Delayed seizure activity following enflurane anesthesia. *Anesthesiology*, 1975; **42:** 367–8.
3. Jenkins J, Milne AC. Convulsive reaction following enflurane anaesthesia. *Anaesthesia* 1984; **39:** 44–5.
4. Spence AA. The halothane-liver controversy. In: Lunn JN, ed. *Epidemiology in anaesthesia.* London: Edward Arnold, 1986: 74–92.

Analgesia for neonates

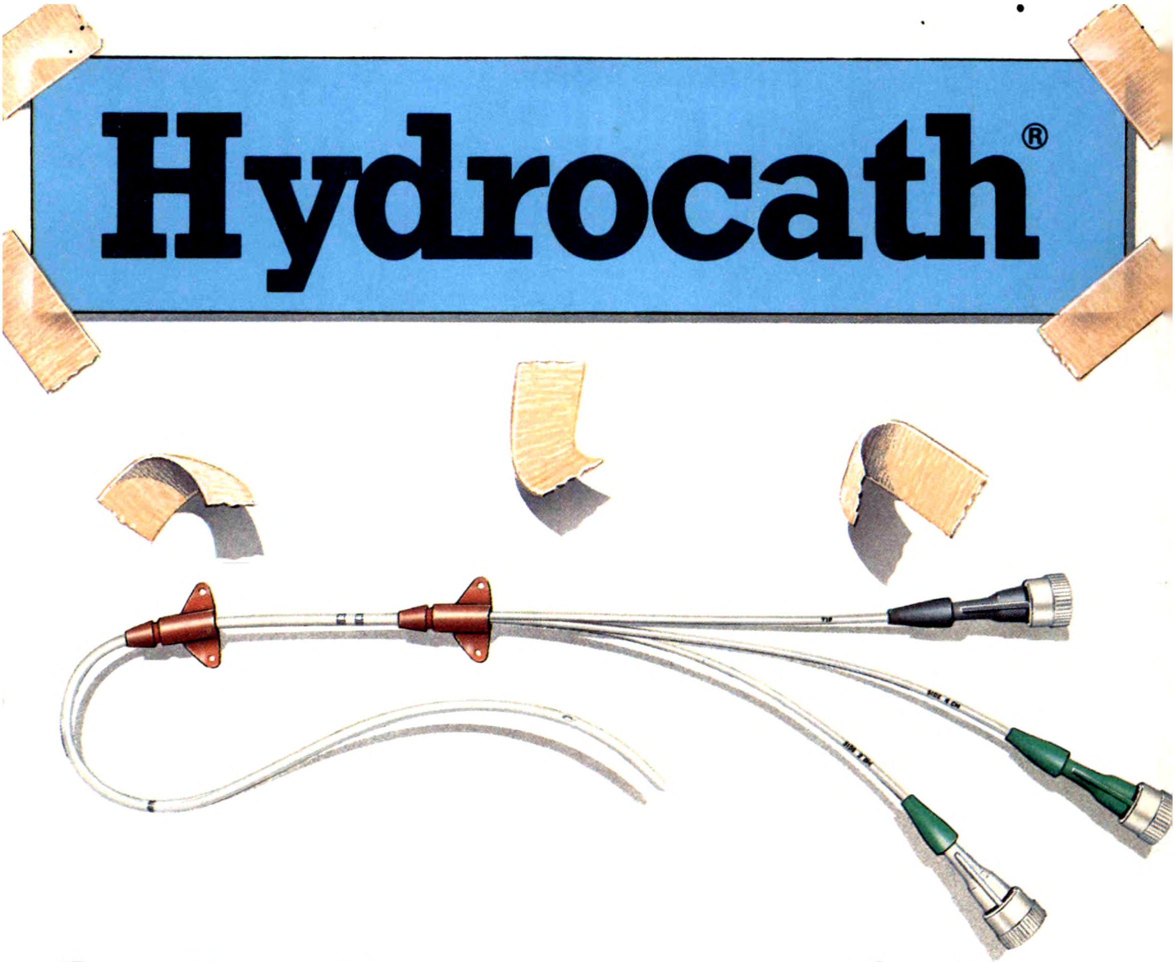
The editorial by Dr Booker on postoperative analgesia for neonates (*Anaesthesia* 1987; **42:** 343–5) gave a good and reasoned discussion of whether or not neonates feel pain. It is good that at last this topic is receiving the attention that it deserves.

It seems to me that we have to be honest and decide exactly why 48% of paediatric anaesthetists do not administer postoperative (or indeed intra-operative) analgesics. If they genuinely believe that neonates do not feel pain, then one can perhaps understand their reluctance to provide any sort of analgesia. This would also apply to those who do not administer adequate anaesthesia, as observed by Anand and Aynsley-Green[1] who found that 77% of neonates undergoing ligation of patent ductus arteriosus received either muscle relaxants or relaxants with nitrous oxide as the sole anaesthetic. If, as the evidence now seems to suggest, neonates not only feel pain but mount a considerable catabolic response to surgical stress, then the only excuse for not using intra-operative and/or postoperative narcotics (or some form of local analgesic block) is fear of postoperative side effects, the most feared of which is apnoea.

Several studies have examined the incidence of apnoea following anaesthesia.[2–4] These indicate that the incidence of apnoeic episodes increases with increasing prematurity. Apnoea occurs after almost all anaesthetic agents and does not seem to be specifically associated with one agent. Gregory and Steward[5] recommended that elective surgery in premature infants be avoided under 44 weeks postconceptual age but this solution is only of limited usefulness, since many of the procedures (such as inguinal herniotomy) are viewed as emergencies.

The answer is surely to turn our full attention to the postoperative care of these babies. Those at risk, particularly the ex-prems should, where possible, have their surgery only in centres with full neonatal intensive care facilities. They should be cared for by nurses who are fully trained in the specific problems of this group of patients. There should be an anaesthetist or paediatrician immediately available with the skills to intubate the trachea, and the nurses should be trained to ventilate with a bag and a mask until medical help arrives. This already occurs in many special care baby units where permanent on-site medical help is not available.

We should monitor the patient adequately. There are now available reliable transcutaneous oxygen and carbon dioxide monitors, pulse oximeters and a variety of apnoea and ECG monitors. Most of them now have fail-safe alarm systems. It has been suggested that



Only the name sticks.

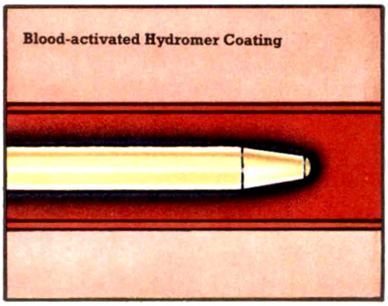
HYDROMER® is the special hydrophilic polymer that protects all HYDROCATH® catheters. When activated by body fluids it creates an aqueous complex which surrounds the catheter.

This complex reduces the surface friction of the catheter to less than that of wet glass, making insertion easier and reducing patient trauma.

Once in situ the Hydromer coat remains activated, creating a barrier at the blood/catheter interface.

For more information on the complete range of Secalon® Hydrocath central venous catheters please telephone (0793) 641791 or write to "Hydrocath", Viggo, P.O. Box 77, Swindon, Wiltshire, U.K.

® = Registered Trademark

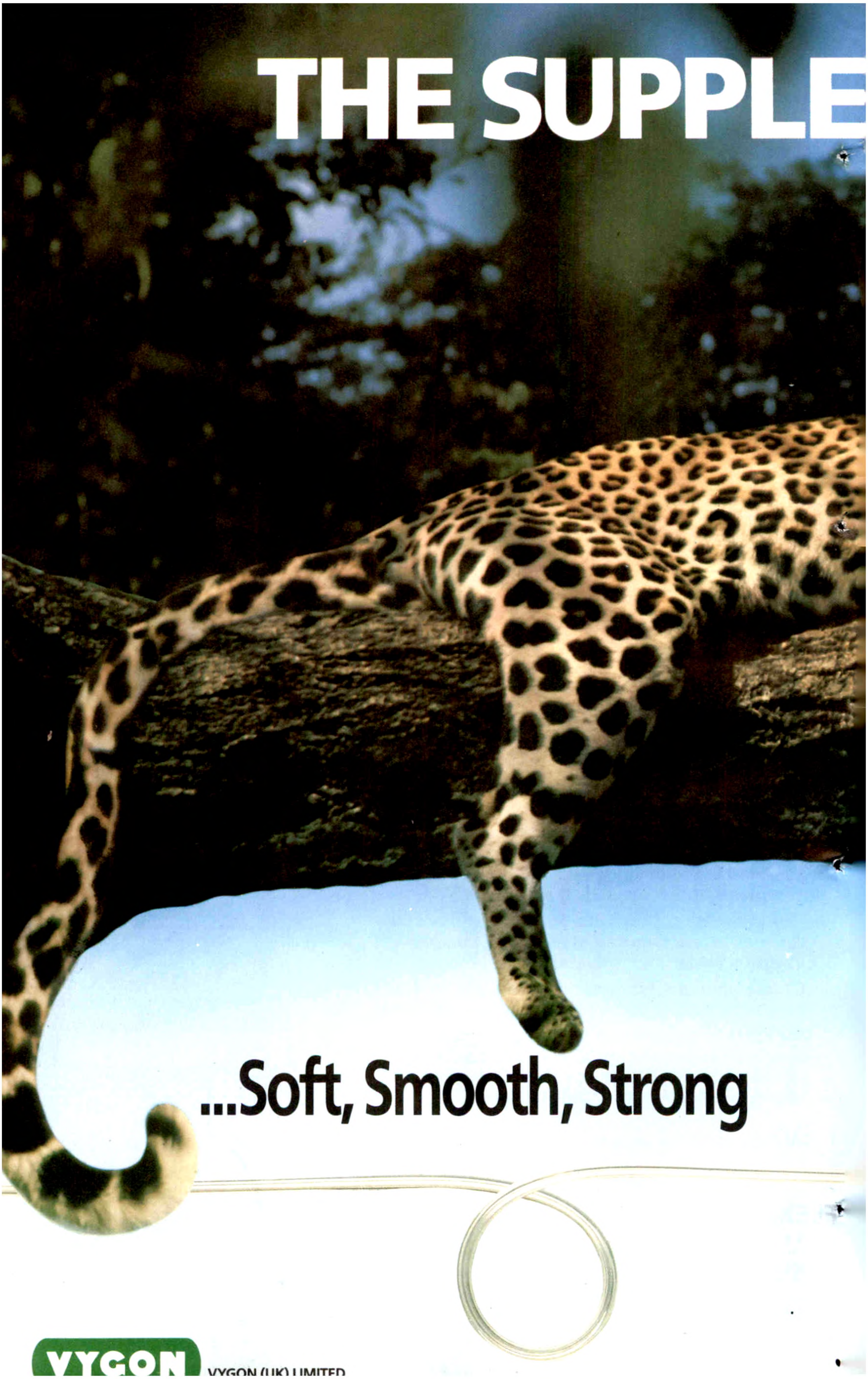


Viggo

British Viggo
Faraday Road
Swindon
Wiltshire SN3 5HZ
Tel: 0793 641791
Telex: 444443 VIGGO G

BOC Health Care

Viggo International Sales
Chertsey Road
Windlesham
Surrey GU20 6HJ
Tel: 0276 77222
Telex: 859363 BOC GHQ G
Fax Nos: 0276 71333/77550



VYGON (UK) LIMITED

FLEXANE™

DEVELOPED TO OUTPERFORM ALL OTHER CATHETER MATERIALS

FLEXANE™ IS USED IN THE MANUFACTURE OF MULTICATH TRIPLE AND DOUBLE LUMEN CENTRAL VENOUS CATHETERS

FOR FURTHER DETAILS ON MULTICATH, COMPLETE AND RETURN THIS COUP

VYGON
VYGON (UK) LIMITED
BRIDGE ROAD, CIRENCESTER, GLOUCESTERSHIRE GL7 1PT

A3

Name ____________________

Title ____________________

Hospital ____________________

Dept. ____________________

City ____________________

Pain management in hospital and the home

Spembly Medical is foremost in the discipline of Pain Management. The Company has earned a unique reputation for its development of high quality instrumentation, particularly for the techniques of Cryoanalgesia and TENS.

An excellent example is the SL2000 Lloyd Neurostat. It adds a new perspective to the management of both acute and chronic pain via localised freezing of nerves. Treatment by Cryoanalgesia is of particular benefit for relieving post-operative pain and in conditions such as facet rhizolysis, coccydynia and neuroma formation.

Equally, the Spembly Medical 140 Cryounit, used in conjunction with the Maiwand probe, is an established method of freezing the intercostal nerves prior to closing the thorax — a recognised means of providing post-thoracotomy pain relief.

Obtaining pain relief, without recourse to drugs, through treatment by TENS is rapidly increasing. Outstanding for this technique is the Pulsar range — a family of small, lightweight battery operated units which enable more patients to obtain greater benefits from TENS over a wider range of clinical conditions. Significantly, Spembly Medical is the first to have designed a special unit for use in Obstetrics.

Spembly medical

Spembly Medical Limited
Newbury Road, Andover, Hampshire,
SP10 4DR, England
Telephone: (0264) 65741 Telex: 47403

Spembly Medical Pain Management products are UK manufactured.

Please clip and return this coupon to Spembly Medical Limited,
Newbury Road, Andover, Hampshire, SP10 4DR, England, for more details on:—

GP/A/12

☐ SL2000 Lloyd Neurostat ☐ 140 Cryounit ☐ TENS Pulsar ☐ Obstetric Pulsar

NAME ______________________ POSITION ______________________

ADDRESS ____

____

______________________ TELEPHONE ______________________ prolonged apnoea can remain undetected despite modern monitoring systems[6] but it is hard to envisage that this could occur with pulse oximeters. Most of them indicate when they are detached and show a saturation only when a pulse is detected. False positives do not therefore occur. A vigorous child who kicks off the probe is not in danger of apnoea, whereas an apnoeic child is quiet and flaccid, under which conditions the most reliable recordings are obtained.

Dr Booker advocates the use of local anaesthetic blocks. The use of local anaesthesia is increasing in some parts of the world. Ilio-inguinal blocks for herniotomy are relatively easy to perform and the quantities of agent required should not have any adverse effects. There have been several recent reports on the use of spinal[7,8] and epidural[9] blocks in neonates, and these techniques may prove to be a safe alternative or adjuvant to general anaesthesia in the high-risk child. More attention should perhaps be paid in Britain to this approach.

Narcotic analgesics can be and are used safely in this group of patients,[10,11] although extreme care should be taken with premature infants. Lower doses or continuous infusions would seem to be the answer, in conjunction with careful monitoring of the child as mentioned above. Alternatively, the newer agonist/antagonist analgesics may prove useful. There has been considerable research in recent years into the kinetics and dynamics of narcotic analgesics, and the appropriate application of this information should increase the safety of these agents.

We must face up to the reality that neonates require considerably more intensive postoperative care, which applies whether or not narcotic analgesics are used. This may mean centralisation of neonatal anaesthetic care. It will certainly mean more expenditure to upgrade facilities. This may be an unpopular economic option but the nettle must be grasped if we are to proceed to the end of this century providing effective anaesthetic care to this group of patients who are unable to communicate their feelings to us.

Bristol Royal Hospital
for Sick Children,
Bristol BS2 8BJ

I.S. Gauntlett

References

1. Anand KJS, Aynsley-Green A. Metabolic and endocrine effects of surgical ligation of patent ductus arteriosus in the human preterm neonate: are there implications for further improvement of postoperative outcome? *Modern Problems in Paediatrics* 1985; **23**: 143–57.
2. Steward DJ. Preterm infants are more prone to complications following minor surgery than are term infants. *Anesthesiology* 1982; **56**: 304–6.
3. Liu LMP, Cote CJ, Goudsouzian NG, Ryan JF, Firestone S, Dedrick DF, Liu PL, Todres D. Life-threatening apnea in infants recovering from anesthesia. *Anesthesiology* 1983; **59**: 506–10.
4. Kurth CD, Spitzer AR, Broennle AM, Downes JJ. Postoperative apnea in preterm infants. *Anesthesiology* 1987; **66**: 483–8.
5. Gregory GA, Steward DJ. Life-threatening perioperative apnea in the ex-'premie'. *Anesthesiology* 1983; **59**: 495–8.
6. Hatch DJ. Analgesia in the neonate. *British Medical Journal* 1987; **294**: 920.
7. Harnik EV, Hoy GR, Potolicchio S, Stewart DR, Siegelman RE. Spinal anesthesia in premature infants recovering from respiratory distress syndrome. *Anesthesiology* 1986; **64**: 95–9.
8. Abajian JC, Mellish RWP, Browne AF, Perkins FM, Lambert DH, Mazuzan JE. Spinal anesthesia for surgery in the high-risk infant. *Anesthesia and Analgesia* 1984; **63**: 359–62.
9. Dalens B, Tanguy A, Haberer JP. Lumbar epidural anesthesia for operative and postoperative pain relief in infants and young children. *Anesthesia and Analgesia* 1986; **65**: 1069–73.
10. Koren G, Butt W, Chinyanga H, Soldin S, Tan YK, Pape K. Postoperative morphine infusion in newborn infants: assessment of disposition characteristics and safety. *Journal of Pediatrics* 1985; **107**: 963–7.
11. Duncan A. The postoperative period. *Clinics in Anaesthesiology* 1985; **3**: 619–32.

Preferential oxygen leak—an unusual case

The potential of the usual arrangement of Rotameters on an anaesthetic machine to give a preferential loss of oxygen in the event of a leak in the Rotameter block is well known.[1] We report a leak which resulted in delivery of an hypoxic mixture to patients, which would not have been prevented by baffle channelling of the back bar and was not detected by the manufacturer's present test procedures following a service or by routine pressure testing of the anaesthetic machine.

A Boyle International Mk1 anaesthetic machine (BOC Medical) was serviced by the manufacturers and returned to use. Our usual pre-use checks (which do not at present include an inspired oxygen test) did not reveal any problems. In particular, the usual daily pressure test which involves the occlusion of the common gas outlet, did not reveal any apparent leaks in that the pressure relief valve opened and the Rotameter bobbins were depressed in the usual manner. It was noticed 2 weeks later that a patient connected to the machine appeared cyanosed during controlled ventilation with a Manley Pulmovent (Blease Medical). The cyanosis resolved with manual ventilation and the problem was thought to be related to the tracheal tube. The same problem recurred with a subsequent patient and the machine was withdrawn from service for checking.

Examination of the machine showed that with the

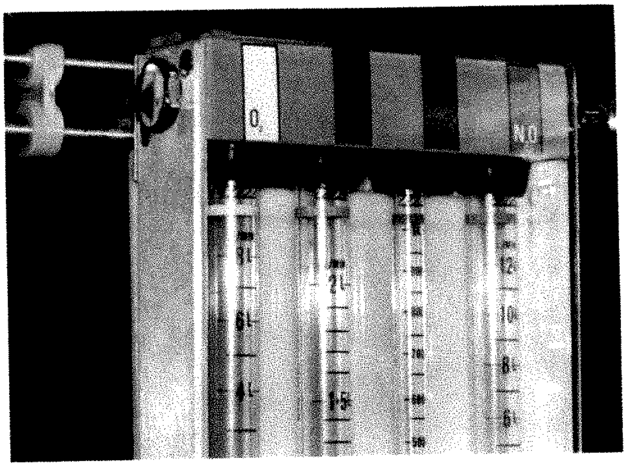


Fig. 1. Rotameter block of Boyle International anaesthetic machine (BOC Medical) showing the blanking plug.

Rotameters set to deliver 33% oxygen the inspired oxygen concentration ($F\text{IO}_2$) at the common gas outlet was 0.3 with nothing attached. The addition of a spontaneous breathing system reduced the $F\text{IO}_2$ to 0.28, and connexion of the ventilator in the automatic mode, to between 0.1 and 0.15. The degree of reduction in $F\text{IO}_2$ was proportional to the resistance offered to gas flow by the system and thus to the pressure in the back bar. The source of the leak was found to be a loose blanking plug at the left-hand end of the back bar (Fig. 1) and tightening the plug corrected the reduction in $F\text{IO}_2$.

The blanking plug is used by the manufacturers to connect a pressure gauge as part of the testing of the integrity of the back bar after a service. We assume, although we cannot be certain, that the plug was not replaced tightly after this test. The final test at the completion of a service is to attach an oxygen analyser to the common gas outlet. However, this test is performed without a breathing system attached so that the pressure in the back bar remains low and the leak was not detected. The presence of the leak was not suspected from the daily checks since it was relatively small. The leak would only have been about 1 litre/minute with a typical fresh gas flow rate of 7.5 litres/minute (2.5 litres/minute of oxygen and 5 litres/minute of nitrous oxide) if it is assumed that pure oxygen was lost. Such a loss would not cause significant hypoventilation and did not prevent depression of the Rotameter bobbins on occlusion of the common gas outlet.

Four lessons are apparent from this incident. Firstly, the investigation of any unexplained cyanosis must include an examination of the anaesthetic machine. Secondly, the inability of the human eye to detect hypoxia is again confirmed;[2] the machine was in use for 2 weeks before the fault was detected. Thirdly, this fault would have been detected immediately had oxygen analysers been in routine use and fourthly, the testing of delivered oxygen concentrations must be performed with the back bar pressure held above the normal working pressure. The Manley ventilator increases the back bar pressure to between 120 and 150 kPa so a test pressure of 200 kPa is recommended.

The General Hospital,
Leicester LE5 4PW

C.D. Hanning
D. Kruchek
A. Chunara

References

1. Ward CS. *Anaesthetic equipment*, 2nd edn. Eastbourne: Baillière Tindall, 1985: 47–8.
2. Hanning CD. Monitoring oxygenation during anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 359–60.

A reply

We thank the Editor and the authors of this letter for bringing the above matter to our attention and for affording us the opportunity to reply.

The points made in the letter have been noted and will be looked into. We concur with the recommendation in their final paragraph.

P. Sim

Ohmeda,
Elizabeth Way,
Harlow,
Essex CM19 5AB

Gross hypernatraemia associated with the use of antiseptic surgical packs

It was surprising to read the article on hypernatraemia (*Anaesthesia* 1987; **42**: 750–3) which not only gave inadequate data to assess the case but almost certainly was wrong to ascribe the cause to the intravenous solutions used.

Hypernatraemia is common in poorly controlled intravenous nutrition and this is almost certainly the cause in this case. When protein is broken down and urea is formed, the ketogenic or glucogenic residue of the amino acid enters energy metabolism. Twenty grams of nitrogen breakdown per day provides approximately 500 cal and in one bizarre case 1500 cal were provided from this source. No information was given on nitrogen breakdown but it would be expected to be high.

This patient received in addition 2000 cal of carbohydrate input per 24 hours and this almost certainly would have exceeded the patient's requirements.[1] No indication is given of the patient's energy requirements from indirect calorimetry but the glucose load together with the energy provided by the protein metabolism almost certainly would have been excessive. That this was so in this case is suggested by the requirement to use insulin (dose not given, glucose levels not given). It is rare to require insulin if the patient's energy input is balanced against their energy requirements.

The excess glucose and metabolites increase intracellular osmolarity and cause water to move into the intracellular compartment; the increased osmolarity is reflected in an increase in the serum sodium in the depleted extracellular space.[2–4] This might have been reflected in a high MCV if the change was not obscured by transfusion.[5]

The correct management is to match the energy input to the patient's requirements and to be aware of this and never to allow the sodium to go above 150 mmol/litre. If the patient does become hypernatraemic then intravenous nutrition should be stopped until the excess carbohydrate load has been metabolised. This causes the decrease in serum sodium observed when intravenous nutrition was discontinued in this case. The administration of 5.5 litres 5% dextrose was unnecessary and the decrease in serum sodium thus induced was dangerously rapid in an already potentially lethal state.

It is regrettable that the patient's weight was not given, that total fluid balance was not measured by weight change and that sodium balance on a daily basis was not included, nor the sodium content of the blood products and antibiotics given. It should also be pointed out that the use of Vamin 18 (electrolyte free) would have enabled the sodium input to be considerably less than the 72 mmol/day quoted.

Intensive Care Unit,
Royal Infirmary,
Cardiff CF2 1SZ

C.C. Wise

References

1. Burke JF, Wolfe RR, Mullany CJ, Mathews DE, Bier DM. Glucose requirements following burn injury. Parameters of optimal glucose infusion and possible hepatic and respiratory abnormalities following excessive glucose intake. *Annals of Surgery* 1979; **190**: 274–85.
2. MacFie J, Smith RC, Hill GL. Glucose or fat as a nonprotein energy source? A controlled clinical trial in gastroenterological patients requiring intravenous nutrition. *Gastroenterology* 1981; **80**: 103–7.
3. Prescott RWG, Stoddart JC. Unrecognised dehydration during parenteral nutrition. *British Medical Journal* 1980; **280**: 847.
4. Wise CC. Unrecognised dehydration during parenteral nutrition? *British Medical Journal* 1980; **280**: 1086–7.
5. Allen SC, Balfour IC, Wise CC. The red cell osmometer. A useful inaccuracy in measurement of mean corpuscular volume in hyperosmolar states. *Journal of Clinical Pathology* 1980; **33**: 430–3.

A reply

We thank Dr Wise for his interest and comments on this complex case. Much detail was omitted in the case report, in the interests of brevity and clarity. Briefly, the omitted data that Dr Wise would have liked are as follows.

The measured nitrogen loss was indeed high at 20–25 g nitrogen/day. A sliding scale of insulin was in use with an average of about 4 units/hour to maintain a blood glucose of 10 mmol/litre or below, although at times higher levels were recorded. We do not possess a weigh-bed; the patient was 6′ 3″ and of average build and was assumed initially to weigh 80 kg. Sodium balance was not included because it would have been meaningless with sodium loss in diarrhoea in the early stages, sweat and blood loss from the wounds being unrecordable. The average daily parenteral sodium input stated in the text to include drugs, did include parenteral antibiotic therapy. We assumed that the sodium content of blood product was similar in all parts of the United Kingdom, i.e. human plasma protein solution 130–150 mmol/litre and packed cells similarly about 14 mmol/pack if each unit of packed cells contains approximately 100 ml of anticoagulant and plasma.

We do not consider an input of 2000 calories of carbohydrate/day to be excessive in a septic patient, allowing 140–200 calories/g nitrogen. Where possible both fat and carbohydrate are used as calorie sources. In our experience insulin is commonly required when 50% dextrose is used, in order to maintain blood glucose below the renal threshold; a diabetic-like state is common in stressed patients. We do not see hypernatraemia as a regular consequence of this therapy. Dr Wise's contentions that the carbohydrate input was excessive and that this caused extracellular dehydration are not totally supported by the research to which he refers. His first reference[1] investigated three dose levels for glucose infusion. 2000 calories is within the low rate range of 1.5–4.5 mg/kg/minute and would not be considered excessive. In addition, Burke's patients were all in positive nitrogen balance nearly all the time, whereas our septic patients are rarely so. His second reference,[2] far from supporting the statement that precedes it, states within the text that they encountered 'no problems either practical or biochemical with the use of glucose as the only calorie source' and hypernatraemia is not mentioned.

We consider there is neither clinical nor documentary evidence to support Dr Wise's theory on the origin of our patient's hypernatraemic state. Furthermore, our patient received a further week of the same nutritional regimen after discontinuation of Eusol substitute packing and before his demise, without further hypernatraemia. Our references do support the view that fluid and electrolyte movement does occur across large, raw surface areas in contact with dressings. We remain convinced that our own view of the fluid movements in this case holds more water than that of Dr Wise!

Monklands District General Hospital,
Airdrie ML6 0JS

J.M. Thorp
I. MacKenzie
E. Simpson

References

1. Burke JF, Wolfe RR, Mullany CJ, Mathews DE, Bier DM. Glucose requirements following burn injury. Parameters of optimal glucose infusion and possible hepatic and respiratory abnormalities following excessive glucose intake. *Annals of Surgery* 1979; **190**: 274–85.
2. MacFie J, Smith RC, Hill GL. Glucose or fat as a non-protein energy source? A controlled clinical trial in gastroenterological patients requiring intravenous nutrition. *Gastroenterology* 1981; **80**: 103–7.

Ventolin nebules

A male asthmatic patient received controlled ventilation of the lungs after emergency surgery for a ruptured oesophagus. He developed bronchospasm which was treated with intermittent nebulised salbutamol. The ventilator used was a Siemens Servo 900C and the nebuliser was Bird, placed in the inspiratory limb of the ventilator system adjacent to the Y-piece and driven by a continuous additional flow of 4 litres/minute of oxygen.

The expiratory flow transducer in the ventilator started to malfunction after a number of uneventful days of ventilation and nebuliser therapy. The expiratory minute volume exceeded the maximum on the scale despite clinically unchanged ventilation. The patient was ventilated manually with an Ambu bag and the ventilator examined. The expiratory flow transducer was removed and found to be caked with a salty-tasting encrustation. It was replaced with the spare, and mechanical ventilation continued uneventfully. The patient was ventilated adequately at all times.

We found that the hospital pharmacy had recently, in the interests of economy, replaced ward supplies of Ventolin respirator solution with Ventolin nebules: the cost of drug per dose is lower in the nebule formulation. The ventilator malfunction occurred some four treatments after the use of nebules was commenced on the intensive care unit. It had not been appreciated that the ventolin nebule contains a solution of salbutamol in normal saline, whereas the respirator solution is salbutamol in water. Clearly, some of the mist had settled on the expiratory flow transducer, the water had evaporated (the expiratory flow transducer in this ventilator is heated electrically to prevent condensation of water) and left behind an encrustation of salt which eventually caused the malfunction. It is timely to warn colleagues of this particular problem and of the need to be aware of changes in the presentation of commonly used drugs.

Masterton Hospital,
Private Bag,
Masterton,
New Zealand

D.S. Mackie

Intratracheal pressure during controlled ventilation in infants

Synnott, Wren and Davenport (*Anaesthesia* 1987; **42**: 719–26) described an elegant computer method to measure intratracheal pressure that, in essence, corrects for the pressure drop along the tracheal tube when flow is present. As might be expected, this correction becomes more important when flow is great but there are two factors that may reduce its value.

First, the resistance of a tracheal tube assessed in isolation in the laboratory is greater than the resistance of the same tube when it is in place in the upper airway. The authors may have recognised this possibility when they referred to end effects but do not seem to have accepted its importance: the fluid dynamics of the combination of tube and trachea are complex and were described by Chang and Mortola.[1] The pressure in the tracheal tube that they measured is not the same as the pressure within the airway.

Second, the method of Bland and Altman[2] for comparison of measurements by two methods is a valuable technique but is it appropriate when a systematic difference is expected *a priori*? Such a systematic difference, always positive (i.e. peak ventilator pressure greater than peak intratracheal pressure, as expected) and increasing as the mean of the estimates increases (as expected), is demonstrated in the plot in their Fig. 3(a). In addition, such a plot does not reveal what is of great clinical relevance, which is how peak intratracheal pressure (or the computer calculated pressure) is related to pressure in the airway when flow ceases: the pressure in the airway then decreases because flow into the lungs has stopped. Only if the airway resistance is great, will there be a great difference between the peak and pause pressures measured at this point. In fact, the difference between peak and pause pressures measured by the dial on the ventilator represents the flow resistance of the tube and respiratory system in series: for this reason, many clinicians believe that both the peak and pause pressures are important values to note. In the infants and children studied, how great was the difference between computed peak and the pause pressure, which would indicate the flow resistance of the patient's respiratory system? If there was little, then there can be little advantage in attempting to calculate intratracheal peak pressure rather than the more simply measured pause pressure which indicates the pressure throughout the inflated lungs (and may well be better related to barotrauma than the peak pressure). Certainly, the peak tracheal pressure in the test lung did not increase greatly as flow increased and one suspects that the same was true in the patients studied.

Finally, how is it possible to explain an error in pressure measurement caused by compression volume in the ventilator tubing? Is this intended to describe the very small flow of gas into this tube caused by compression of the gas within the tube, and hence a pressure difference set up by this flow in the small resistance of the ventilator tubing? Or is it, more probably, caused by a difference in time constant due to the interposition of the compliant tubing? A pressure gradient is not truly set up by a compressible volume (compliance): pressure gradients are caused by flow.

Many of these confounding factors could be avoided by measuring pressure when no flow in the apparatus was present, that is, in a pause at the end of inspiration, which could easily be imposed, even temporarily, with the controls of the Servo 900C.

Royal Infirmary,
Edinburgh EH3 9YW
G.B. Drummond

References

1. Chang HK, Mortola J. Fluid dynamic factors in tracheal pressure measurement. *Journal of Applied Physiology* 1981; **51:** 218–25.
2. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1:** 307–10.

A reply

Thank you for the opportunity to discuss the interesting points raised in Dr Drummond's letter. We agree that the effective resistance of the tracheal tube measured in isolation differs from its resistance when placed in the patient's airway. However, we have found the effects due to this difference to be small relative to the effect of flow through the tube. This finding is, perhaps, not surprising since our work was carried out mostly on babies in whom the effects described by Chang and Mortola[1] would be expected to be minimised due to the relatively small difference between the internal diameters of the tracheal tube and trachea, the relatively high respiratory frequency and the expected relatively low value of mean Reynold's number for tracheal flow. Moreover, as outlined in the appendix of our paper, some account was taken of this effect in the bench tests used to establish the pressure–flow relationships of the Portex tubes. So while we accept that the pressures yielded by our method may not precisely reflect pressure in the airway, we contend that the difference is unlikely to be of major clinical significance. The situation in adults may, of course, be different since the difference between tracheal tube diameter and tracheal diameter is usually greater in adults.

The main purpose with regard to the statistical methods used, was to compare the results obtained using our computer method with results obtained by direct measurement in the airway. In this case there were no *a priori* expectations so the objections raised do not apply. This method was used to compare computer predictions with direct measurements so it seemed appropriate, for the sake of clarity, to use the same method to compare ventilator breathing system pressure measurements with direct measurements.

The third and, in our view, most important point, concerns the use of pause pressure. Our method yields information about airway pressure throughout the inspiratory phase (not just peak pressure), whereas pause pressure is measured at a single instant at the end of an imposed inspiratory pause. It is thus a static measurement of a dynamic event. Precisely what pause pressure reflects must depend on a relationship between the duration of the imposed inspiratory pause and the patient's airway resistance. If the duration of the pause is relatively long and pressure in the lung equilibrates rapidly, then pause pressure will indeed reflect pressure throughout the inflated lung and probably yield valuable information. This is likely to occur in healthy adults with low airway resistance whose lungs are ventilated at low respiratory frequency with relatively long inspiratory pauses. It seems less likely to be true in sick neonates ventilated at higher frequencies, and very unlikely during HFPPV where it is practically impossible to impose an inspiratory pause of significant duration. Thus pause pressure reflects different things in different clinical situations and it is difficult for the clinician to be certain what it reflects in any specific circumstance. It also necessitates the imposition of an inspiratory pause, a manoeuvre which may not always be appropriate from a purely therapeutic point of view and may not be possible in certain modes of ventilatory support. Moreover, the facility to measure pause pressure simply, is not incorporated into all ventilators. Our method does not suffer from these limitations.

Finally, we take issue with the idea that pause pressure may be better related to barotrauma than peak pressure. There are in our view insufficient data available to draw valid conclusions on this issue. There is clearly a need for a large prospective study to investigate the relationships (if any) between airway pressures measured by different methods (peak and mean pressures measured directly in the airway, peak and mean pressures calculated by our computer method and peak, mean and pause pressures measured in the ventilator breathing system) and the incidence of barotrauma. We are in the process of setting up such a study and will report our findings in due course.

Our Lady's Hospital for
Sick Children,
Crumlin,
Dublin 12,
Ireland

A. Synnott
W.S. Wren
J. Davenport

Reference

1. Chang HK, Mortola J. Fluid dynamic factors in tracheal pressure measurement. *Journal of Applied Physiology* 1981; **51:** 218–25.

Auto-antagonism of buprenorphine

Dr Molke Jensen and his colleagues (*Anaesthesia* 1987; **42:** 470–5) have most elegantly demonstrated biphasic respiratory depression in volunteers following epidural buprenorphine.

There is one possible explanation of this phenomenon that they overlook, namely that buprenorphine can antagonise itself. Thus when the peak effect might be expected, inhibition occurs. A very similar biphasic antinociceptic response due to auto-antagonism with a large systemic dose of buprenorphine was demonstrated in rats by Dum and Herz.[1]

St Thomas' Hospital,
London SE1 7EH

F. Reynolds

Reference

1. Dum JE, Herz A. *In vivo* receptor binding of the opiate partial agonist, buprenorphine, correlated with its agonistic and antagonistic actions. *British Journal of Pharmacology* 1981; **74:** 627–33.

Editor's note. The authors agree with this suggestion.

Unstable cervical fracture

The report of J.R. Eason *et al.* (*Anaesthesia* 1987; **42:** 745–9) which described anaesthesia for urgent Caesarean section in a patient with an unstable cervical fracture was interesting. One may agree that the unique and conflicting requirements of this case make management difficult but the technique described appears to suffer from a number of inherent shortcomings.

How was it proposed to deal with vomiting or with regurgitation (not invariably controlled by cricoid pressure) during induction when the patient was immobilised in the supine position? Application of adequate cricoid pressure and direct laryngoscopy would risk both inadvertent neck movement (even for a C_2 fracture) and consequent spinal cord injury.

These limitations would be overcome by skilled awake fibreoptic intubation and, as the authors note, this would be the method of choice in North America. Surely their comments that 'this would have been the safest technique' but that 'few anaesthetists are so skilled in its use that they would unhesitatingly employ it . . .,' are an indictment of our attitude to and training in this technique?

The Hospital for Sick
Children,
Great Ormond Street,
London WC1N 3JH

N. Braude

A reply

Thank you for the opportunity to reply. We realised our choice of technique was open to criticism but we felt we should go ahead and report the case since this patient presented such an unusual problem.

We agree that fibreoptic awake intubation is not used as often as it should be in British anaesthetic practice. Perhaps as a result of this, the fibreoptic intubations we have witnessed or performed ourselves have always involved a good deal of coughing and straining despite liberal use of sedation and local anaesthesia. The staff in our chest clinic, who are considerably more experienced than ourselves, tell us that they have the same problem. It may be that an adept practitioner such as Dr Braude could have achieved tracheal intubation smoothly in this patient but, as we indicated in our report, she was a large lady, lying supine in skull traction and she was very distressed (and therefore uncooperative).

Dr Braude rightly draws attention to the risk of vomiting during induction and intubation. This would have been a nightmare and we had an assistant whose sole responsibility it was to hold two working suckers, one with and one without a Yankauer attachment, ready to hand. Mercifully, not every obstetric patient vomits: had this patient done so, prompt suction under direct vision was all we had to offer.

We considered that the risk of tetraplegia took precedence over the risk of aspiration. We do not accept that cricoid pressure and laryngoscopy, as we performed them, caused any movement at the fracture site. The laryngoscope was inserted with great care and the temptation to improve the view of the larynx by moving the patient's neck (which was firmly wrapped on three sides with a rigid Vak-Pak and was held in 4.5 kg traction with an orthopaedic surgeon holding the head and shoulders) was resisted.

We respectfully suggest that even the most expert endoscopist, faced with this patient as she presented to us, might have thought twice before inserting his bronchoscope.

King's College Hospital,
London SE5 8RY

J.R. Eason
C.N. Swaine
P.I.E. Jones

A new ventilator for closed breathing systems

The paper by Dr Twigley *et al.* (*Anaesthesia* 1987; **42:** 419–24) which described the OAV 7700 ventilator from Ohmeda was a good review of the positive aspects of this basically sound machine. In addition to its role in controlled ventilation, the machine is advertised to have the capacities for synchronised intermittent mandatory ventilation (SIMV) and continuous positive airway pressure (CPAP).

Unfortunately, the design places the positive end expiratory pressure (PEEP) valve between the patient and the reservoir bag. In order to generate spontaneous gas flow the patient must overcome any applied positive expiratory pressure before he can open the non-return valve (Fig. 2 in the article) which separates the patient side of the breathing system from the reservoir bag. Anaesthetised patients cannot, in my experience, ventilate spontaneously through this system when any positive pressure is applied to the PEEP valve and, therefore, although the SIMV mode is highly satisfactory without PEEP, neither SIMV with PEEP nor CPAP is feasible using this machine. The synchronisation mechanism depends on the detection of expiratory flow from the patient so this, too, will not function in the presence of PEEP.

The ventilator is otherwise most satisfactory, and the SIMV mode is a useful feature in addition to the controlled ventilation mode described by Twigley and colleagues. However, potential purchasers of this device should be aware of its shortcoming in respect of PEEP, since it is difficult to see how the design problem can be corrected simply without a major alteration in circuit configuration. The manufacturers have been notified of this defect.

Hillbrow Hospital,
Private Bag 23140, Joubert Park,
Johannesburg, South Africa

M.F.M. James

The assessment by Twigley *et al.* of the Ohmeda OAV 7700 ventilator (*Anaesthesia* 1987: **42:** 419–24) was interesting. They claim to have shown a reduced minute volume requirement to maintain isocapnia when the fresh gas flow (FGF) is delivered at the tracheal tube.

However, with the FGF at points 1 and 3 in their Fig. 2 the tidal volume (V_T) delivered to the patient is the bellows volume plus the amount of fresh gas which enters the system when the expiratory valve is closed:

$$V_T = \text{bellows volume} + (1/3 \times 1/12 \times \text{FGF})$$
$$\text{(for I:E ratio 1:2 and frequency of 12)}$$

With the inflow at position 1 both elements are measured as expired tidal volume but with the inflow at position 3 the FGF has to be switched off during the period of V_T measurement in order to identify the end of expiration. The removal of the FGF contribution would result in an underestimation of V_T (using the ventilator settings given in the article in the above formula) of 111 ml at an FGF of 4 litres/minute but only 28 ml at an FGF of 1 litre/minute. Adding these values to the relevant values of V_T given in the article, brings the V_T required to maintain isocapnia when the FGF is delivered at the tracheal tube into the range stated for other sites of FGF delivery.

The apparent increase of efficiency seen by Twigley *et al.* is thus likely to be due to the omission in their measurements of the contribution made by the FGF to V_T.

Western Infirmary,
Glasgow G11 6NT

J.L. Plenderleith

A reply

Thank you for the opportunity to reply to these letters. This ventilator was presented to us by Ohmeda for evaluation solely as a closed system anaesthetic ventilator as which it was designed. In our conclusions we indicated that it provided independent controls for V_T, ventilation frequency, I:E ratio and PEEP and that it would synchronise with the patient if spontaneous breathing occurred. The model we studied was, as far as we are aware, not intended for use as a CPAP device or in an SIMV mode. It is possible that Dr James' comments are relevant to claims by the manufacturers but they do not reflect the content of our paper. Our view of this machine is that it is an interesting new development for mechanical ventilation during closed system anaesthesia.

The contribution of the fresh gas flow (FGF) during the measurement of tidal volume (V_T) was taken into account. The airway pressures which were measured with the FGF flowing during IPPV reflect the decrease in the V_T. When the FGF was supplied in the tracheal tube the stroke volume of the bellows had to be reduced more than the contribution of the FGF during the inspiratory phase to maintain a relatively constant $P\text{aco}_2$. It was not considered essential to publish the details of this manoeuvre for the measurement of V_T. This consisted of adjusting the peak airway volume of the bellows when the FGF was switched off. This was necessary for the measurement not only of the V_T but also the end tidal CO_2 concentration.

Reference to the flow pattern (Fig. 3 in our article) shows that the FGF would scavenge without CO_2 mixing from alveolar gas during the last part of the expiratory phase. At 12 breaths/minute with an I:E ratio of 1:2, approximately 1–1.5 seconds would be expected for this period. The apparatus deadspace including the tracheal tube was approximately 80 ml; therefore, during periods of say 1 second, FGF at 4, 2 and 1 litres/minute can flush only approximately 67, 33 and 17 ml, respectively. It is a complex situation and the effective contribution of FGF depends mainly on the pattern of the expiratory alveolar gas flow and its composition, the apparatus deadspace volume and the FGF rate.

There is a *prima facie* case that removal of the tracheal tube deadspace by scavenging with fresh gas will improve the efficiency of ventilation and hence require a smaller V_T. However, our study shows that at these ventilation frequencies, i.e. 12 breaths/minute, there is little advantage to be gained by complicating the system rather than supplying the fresh gas at the machine in a manner recommended by the manufacturers.

Hammersmith Hospital,
Du Cane Road,
London W12 0HS

A. TWIGLEY
M.K. CHAKRABARTI
J.G. WHITWAM

Air–oxygen mixtures

The paper by Moseley *et al.* (*Anaesthesia* 1987; **42:** 609–12) was interesting. The authors consider that oxygen-enriched air can be substituted for nitrous oxide and oxygen in general anaesthesia without alteration in the quantities or concentrations of other drugs that are administered. That is my interpretation of the sentence in their discussion, 'there is very little difference in the pattern of anaesthesia compared with the use of other drugs', which is the only mention of this aspect of the subject in the paper.

Nitrous oxide is an important component of many modern anaesthetic techniques and if it is omitted then increased amounts of other agents (e.g. halothane) are necessary to maintain surgical anaesthesia. This was our experience in anaesthetising patients without nitrous oxide. It may be that the authors do have information on this subject since their Table 2, which is headed 'Cost effectiveness', shows that the compressed air group received 25% more halothane than the nitrous oxide group, but it is not possible to determine this point without further information on the number of patients, type of ventilation, etc.

The authors have convincingly shown the big financial benefit that results from the banishing of nitrous oxide. Could they now be persuaded to analyse their data to reveal the resulting changes in usage of other drugs?

Northwick Park Hospital,
Harrow,
Middx HA1 3UJ

D.C. WHITE

A reply

Thank you for giving us the opportunity to respond to these comments. We agree that there was a 25% increase in the use of halothane in the group who received compressed air–oxygen compared to the group who received nitrous oxide–oxygen. Statistical evaluation of the data (Student's *t*-test) showed no significant difference in the quantities of drugs (thiopentone, midazolam, flunitrazepam, diazepam, pethidine, morphine and promethazine) used in the two groups.

The higher total cost of morphine in the compressed air group (Table 2) was due to two factors. Forty-one patients (22%) in the nitrous oxide group received morphine compared to 53 patients (29%) in the compressed air group. The cost of the drugs, including morphine, was calculated according to the ampoules used rather than as cost per mg of morphine.

As far as the pattern of anaesthesia is concerned, controlled ventilation was performed in 74 patients (41%) in the compressed air group and in 78 patients (43%) in the nitrous oxide group.

Queen Elizabeth Hospital,
University of West Indies,
Barbados,
West Indies

H. MOSELEY
A.Y. KUMAR
K.B. SHANKAR
P.S. RAO

Reservoir volume in a drawover system

We read with interest the paper on drawover anaesthetic systems by Dr Mackie (*Anaesthesia* 1987; **42:** 299–304) and wish to make the following comments.

The inspired oxygen concentration, as stated by Mackie, depends on the amount of oxygen supplementation and the minute volume, if other variables of the equation remain constant. The volume of the reservoir necessary for efficient use of the oxygen depends solely on the flow rate of supplemental oxygen and the expiratory time. This can, therefore, be calculated theoretically. The volume of the oxygen supplement per breath is the oxygen accumulated in the reservoir during expiration plus the oxygen delivered during inspiration. Considering a theoretical model at two arbitrary expiratory times and an oxygen supplement of 4 litres/minute, the volume of oxygen which accumulates during expiration will be for an expiratory time of 2 seconds, $(4000/60) \times 2 = 133$ ml and for an expiratory time of 6 seconds, 400 ml.

Clinically, expiratory time is unlikely to exceed 6 seconds which supports Mackie's conclusion that the reservoir volume needs to be about 400 ml. However, a reservoir volume in excess of 400 ml is preferable because of the potential loss of oxygen by diffusion. Houghton[1] in the Triservice apparatus used a Laerdal extension tube of 0.75 metres length which had a reservoir volume of about 450 ml.

Dr Mackie found that the experimental values of inspired oxygen concentration were less than those predicted and this was more marked at minute volumes less than 4 litres/minute. Diffusion of oxygen from the reservoir tube could be responsible for this observation. Further work by Houghton carried out in Sheffield by kind permission of Professor Nimmo showed that a bag oxygen reservoir (Laerdal 531901) which incorporated a reservoir valve (Laerdal 531902) produced inspired oxygen concentrations approximately 1–2% higher than the open-ended Laerdal extension tube (Laerdal 871000) and this supports the hypothesis of diffusion loss of oxygen. However, a mass spectrometric study of the Laerdal anaesthetic valve's performance showed that there was some leakage of air through the expiratory side of the valve which, whilst of no clinical importance, could increase the discrepancy between the predicted and experimental values.

B.M.H. Munster,
B.F.P.O. 17,
Germany

S. YOGANATHAN
I.G. JOHNSTON
I.T. HOUGHTON

Reference

1. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36:** 1094–1108.

A reply

The findings we reported are consistent with these comments. The longest accumulation phase studied was 4 seconds ($f = 10$ breaths/minute, I:E = 1:2) and in this case the $F\text{IO}_2$ (adding 4 litres/minute oxygen to the 415 ml reservoir) was less than predicted if it was assumed that no oxygen was lost from the system. An accumulation phase of 6 seconds would require a reservoir significantly larger than 400 ml to make efficient use of 4 litres/minute added oxygen. The air and oxygen in the reservoir are not separated by a sharp, straight boundary so the open-ended reservoir does not behave in an ideal fashion; neither, it appears, does the Laerdal reservoir bag, if only 1–2% improvements in inspired oxygen concentration are achieved.

University of Washington RC76,
Seattle, WA 98195, USA

A. MACKIE

Oesophageal stethoscope

Accurate monitoring during paediatric anaesthesia is essential for patient safety although access can be difficult especially in small infants once surgery has begun. The oesophageal stethoscope is recognised to be an extremely useful monitoring device and its use is considered mandatory in some centres.[1–3] A remote oesophageal stethoscope amplifier as previously described[4] was recently tried at Birmingham Children's Hospital. The advantages of amplification are that there is no loss of signal with distance from the patient, less interference when the signal is transmitted and the signal is received at a site convenient to the anaesthetist. The original device was of limited value because of high frequency feedback that caused squeal,

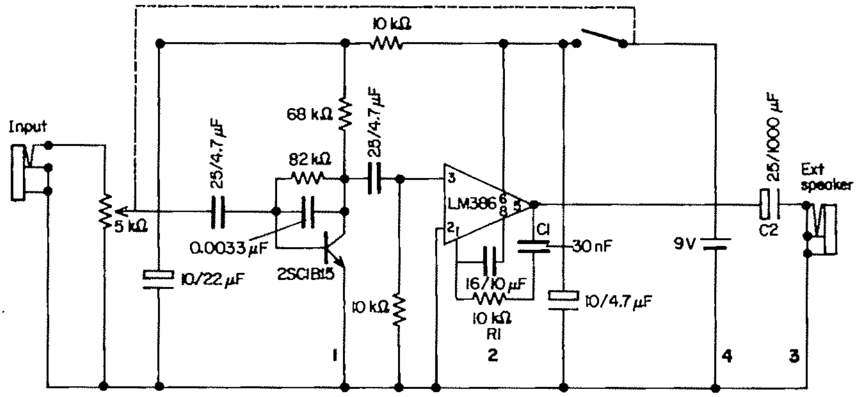


Fig. 1. Bass boost modification to Archer mini speaker amplifier (cat no. 277-1008) (microphone used: Realistic cat. no. 33-1063). 1, Removal of 270 Ω resistor to increase gain of the first transistor stage amplification. 2, Introduction of high frequency negative feedback to give 'bass boost' to op-amp (marked by R1 and C1). 3, Improvement to capacitor coupling to external speaker (marked by C2). 4, Battery changed to 9 volt PP6 to give longer life.

and heart sounds were extremely difficult to distinguish because of a poor low frequency response. We have produced an inexpensive device which is easy to use and has overcome these problems.

The electronic components (Fig. 1), available in any high street, comprise a tie-pin microphone (Tandy cat. no. 33-1063), micro in-ear earphone (Tandy cat. no. 33-977), mini audio amplifier (Tandy cat. no. 277-1008), a 9 volt battery PP6 and other electronic components required for the modifications seen in Fig. 1. These modifications boost low frequency response, reduce high frequency feedback and give a discrete signal through a comfortable earphone. The total cost is under £45.

This device has been used regularly for prolonged procedures in conjunction with disposable oesophageal stethoscope catheters in children and babies of all sizes, from premature neonates to teenagers. The system may also be used with a precordial stethoscope during short procedures in unintubated patients and can be a useful teaching aid for demonstration of normal breathing, partial obstruction and bronchospasm.

Birmingham Children's Hospital,
Birmingham B15 2TH
J. O'Dea
I. Hall

References

1. Gregory GA. In: Sumner E, Hatch DJ, eds. *Pediatric anesthesia.* London, Philadelphia: W. B. Saunders, 1983: 382.
2. Battersby EF. Monitoring during paediatric surgery. *Clinics in Anaesthesiology* 1985; 3: 603–4.
3. Cullen SC. *Anesthesia: a manual for students and physicians,* 6th edn. Chicago: Year Book Medical Publishers, 1961.
4. Douglass R, Doddapaneni B. Esophageal stethoscope amplifier. *Anesthesia and Analgesia* 1985; **64**: 377–8.

Arterial to end tidal carbon dioxide tension difference during anaesthesia for tubal ligation

There is one doubt about the methods in the paper by Dr K.B. Shankar *et al.* (*Anaesthesia* 1987; **42**: 402–6). The carbon dioxide concentrations recorded at the time of arterial sampling were corrected to body temperature and then converted to kPa. Temperature correction for concentration is superfluous. Correction for the loss of water vapour should have been applied since it is known that by the time expired gases reach the proximal end (machine end) of the tracheal tube (site of the carbon dioxide monitor), the temperature of the gases has decreased to 32°C and so the vapour pressure will also decrease as a result of condensation.[1] This needs to be corrected in addition to correction for local atmospheric pressure. The relationship between arterial and end tidal tensions might be a little different if these corrections were applied.

Postgraduate Institute,
2095, Sector 15-C,
Chandigarh 160015,
India
G.D. Puri

Reference

1. Fletcher R, Werner O, Nordström L, Jonson B. Sources of error and their correction in the measurement of carbon dioxide elimination using the Siemens-Elema CO_2 analyzer. *British Journal of Anaesthesia* 1983; **55**: 177–84.

A reply

Thank you for the opportunity to respond to this letter. We do not agree that the corrections made by

BAILLIÈRE'S CLINICAL ANAESTHESIOLOGY

(INTERNATIONAL PRACTICE AND RESEARCH)

Published from 1983 to 1986 as Clinics in Anaesthesiology

Editorial Board M. J. Cousins (Australia), J. F. Crul (Netherlands), O. Norlander (Sweden), J. F. Nunn (UK), L. Strunin (Canada), M. D. Vickers (UK)

Baillière's Clinical Anaesthesiology *is the practical, research-based, international reference you will want to keep. Averaging over 950 pages in total per year, the four hardback, fully illustrated issues provide a reliable and durable resource of current clinical opinion, procedures, techniques and research data. It is the essential reference for all anaesthesiologists who wish to keep abreast of the latest advances in their specialty. Maintaining the exemplary reputation of its precursor,* ***Clinics in Anaesthesiology****, each issue is devoted to a topic of current interest in clinical practice or research.*

March 1987, Vol. 1 No. 1
THORACIC ANAESTHESIA
Editor: J. W. W. Gothard (London)

June 1987, Vol. 1 No. 2
ANAESTHESIA FOR NEUROSURGERY
Editor: D. A. Jewkes (London)

September 1987, Vol. 1 No. 3
ANAESTHESIA AND RELATED SUBJECTS IN BURNS AND PLASTIC SURGERY
Editor: K. C. Judkins (East Grinstead, UK)

December 1987, Vol. 1 No. 4
UPDATE ON OPIATES
Editor: K. Budd (Bradford, UK)

★ Hardback ★ Illustrated ★ 4 issues a year ★ ca 240 pp an issue ★

Annual Subscription: £35.00 (UK & Eire);
(post free) U.S. $60.00 (USA & Canada);
£45.00 (all other areas)

Single issues: £15.00 each (UK & Eire);
(post free) U.S. $25.00 each (USA & Canada);
£18.50 each (all other areas)

Acknowledged by the medical press as bridging the literature gap . . .
"The main merit of such a series lies in the immediacy with which each subject is approached and the fact that the subject matter for each volume represents the response to a perceived need . . . There is a need for a forum of information which bridges the gap between the journals and the standard textbooks. This series bridges this gap admirably within its own field and should be required reading for any clinician who aspires to a special interest in this discipline."

For more details on Baillière's Clinical Anaesthesiology, please write to:
Journals Marketing Department, Harcourt Brace Jovanovich, 3rd Floor, 1 Vincent Square, London SW1P 2PN, U.K.

BAILLIÈRE TINDALL
W.B. Saunders Company

Publications of Interest to
ANESTHESIOLOGISTS

Indispensable tools for maintaining professional competency

ANESTHESIOLOGY

Journal of the American Society of Anesthesiologists, Inc.

Lawrence J. Saidman, M.D., Editor-in-Chief

Anesthesiologists nationwide look to this distinguished journal for current information on all facets of anesthesiology: pharmacologic bases of anesthesia; clinical principles, practices, and techniques; anesthesia management; complications of anesthesia and surgery; and more. The information is published in articles, reviews, current comments, editorial views, case reports, abstracts of current literature, and book reviews.

Published monthly. Individual rate $30.00 per year (U.S.), $69.00 (elsewhere).

REGIONAL ANESTHESIA

Journal of the American and European Societies of Regional Anesthesia

Phillip O. Bridenbaugh, M.D., Editor

For the growing number of those concerned with the burgeoning specialty of regional and local anesthesia, this quarterly journal publishes highly informative articles on the clinical applications of current research and on professional issues and developments.

In addition to original articles, regular features include review articles discussing the current status of particular facets of the field; abstracts from other journals, especially international publications; case reports; clinical reports; correspondence; announcements of professional events; and editorials.

Highlights each year include the full text of the Labat Address, focusing on the humane and philosophical foundations of this field; and the Abbott Lecture, a scholarly and lively look at a particular aspect of regional and local anesthesia and its present implications.

Published quarterly. Individual rate $37.00 (U.S.), $41.00 (elsewhere). Residents $25.00 (U.S. only).

ASA Refresher Courses in Anesthesiology

A Project in the Continuing Education Program of the American Society of Anesthesiologists

Paul Barash, M.D., Editor

Each annual volume in this popular series consists of thirteen to seventeen complete and edited lectures selected from regional and national ASA Refresher Courses. Individually bound, the lecture "chapters" are printed as separate booklets and gathered into an attractively designed looseleaf binder. This format contributes to an orderly file of information for use as a working reference and a continuously updated addition to your personal library. It allows you to tailor it to your own ideas and needs by refiling, reclassifying, or supplementing the material with your own notes, reprints, or other material.

Published annually. Price per volume $15.00 (U.S.), $20.00 (elsewhere). Fourteen volumes are currently available.

PROBLEMS IN ANESTHESIA

A new quarterly series for general anesthesiologists and residents in anesthesia

Robert R. Kirby, M.D., and
David L. Brown, M.D., Editors

NE

Devoted to the daily questions and challenges familiar in the practice of every anesthesiologist: safety for high-risk patients, monitoring, cardiac considerations, OR emergencies, perioperative care. Original, invited articles are directed entirely to *clinical* problems; no research papers or reviews appear. Each volume offers ten to twenty articles, planned by the guest editor or editors and grouped around one or two central themes. Durable, hardbound volumes, generously illustrated, fully indexed, with no advertising, form a permanent and growing library for your permanent reference.

Published quarterly. Individual rate $55.00 (U.S.), $64.00 (elsewhere). Residents $35.00 (U.S. only).

PROBLEMS IN CRITICAL CARE

A new quarterly series for specialists in critical care

NEW!

Robert R. Kirby, M.D., and
Robert W. Taylor, M.D., Editors

Problems—patients with acute, life-threatening conditions—the raison d'etre of every critical care unit. Shock, trauma, drug overdose, cardiac emergencies severe burns—the questions that are familiar in the daily practice of every anesthesiologist who serves as a member of the critical care team. Original, invited articles in this series are aimed foursquare at *clinical* questions, bringing you current information for better care of acutely ill patients. Each volume presents ten to twenty articles, planned by the guest editor or editors and centered around one or two specific topics. Durable hardbound volumes, fully illustrated and indexed, with no advertising, form a permanent resource that will prove its worth through the years.

Published quarterly. Individual rate $55.00 (U.S.), $64.00 (elsewhere). Residents $35.00 (U.S. only).

Lippincott

J. B. Lippincott Company • *The Health Professions Publisher of Harper & Row, Inc.*
East Washington Square, P.O. Box 280, Philadelphia, PA 19105

Please enter my subscriptions to the publications checked:

- ☐ **Anesthesiology**: Individuals $30 (U.S.), $69 (elsewhere).*
- ☐ **Regional Anesthesia**: Individuals $37 (U.S.), $41 (elsewhere);* Residents $25 (U.S.)
- ☐ **ASA Refresher Courses in Anesthesiology**: Vol. 14 - $15 (U.S.), $20 (elsewhere)*
- ☐ **Problems in Anesthesia**: Individuals $55 (U.S.), $64 (elsewhere);* Residents $35 (U.S.)
- ☐ **Problems in Critical Care**: Individuals $55 (U.S.), $64 (elsewhere);* Residents $35 (U.S.)

*Except Japan.

☐ Please send information on previous volumes of the ASA Refresher Courses.

Prices quoted in U.S. funds for individuals only and subject to change.
Orders subject to the approval of Lippincott

Name ______________________
Address ______________________
City/State/Zip ______________________

☐ Residents: To qualify for special rate, please indicate Hospital and Chief of Staff.
____

☐ Payment enclosed. ☐ Please bill me
☐ Charge it: ☐ MasterCard ☐ VISA ☐ American Express
Card No. ______________ Expiration Date ________
Signature ______________________

A1059(

us for end tidal concentrations were superfluous. The main objective of our study was to determine the arterial to end tidal carbon dioxide tension relationship at body temperature. Therefore it was mandatory to correct both arterial and end tidal $P\text{CO}_2$ values to body temperature. It is true that the temperature of expired gases at the site of sampling could be 32°C. Therefore, as was stated in the paper, the partial pressures of carbon dioxide could be higher by 1.5–2% than at body temperature. However, we did not use a Siemens carbon dioxide analyser to measure end tidal concentrations, where the sites of sampling and measurement are the same. As stated in the methods section of our paper, we used a Puritan Bennett Datex CO_2 monitor where the site of sampling is different from the site of measurement. We therefore applied temperature corrections to end tidal concentrations to account for the loss of water vapour during passage from the patient to the monitor according to the instructions given in the reference manual for the Puritan Bennett Datex CO_2 analyser.

The atmospheric pressure was 101 kPa and hence no additional corrections were required for the end tidal concentrations.

Queen Elizabeth Hospital,
University of West Indies,
Barbados,
West Indies

K.B. SHANKAR
H. MOSELEY
Y. KUMAR
V. VEMULA
A. KRISHNAN

Intravenous injections

Frequent puncture of the rubber bung of an intravenous administration set, particularly if made with a large (21-gauge) needle, commonly causes leakage especially if the fluids are to be administered under pressure. Frequent injections are commonly required during anaesthesia and one solution to this small practical problem is to use a short-tailed winged needle which is inserted into the bung. This may have cost advantages over some cannulae but, more particularly, it lessens the risk of accidental removal of the cannula from a vein. In the event of traction on an administration set it will be the winged needle which parts company from the infusion set rather than the cannula from the vein. Furthermore, sterility may be enhanced since the port is less likely to be open to atmosphere and the rubber cap of the winged needle is much easier to clean than is the inlet of a three-way tap or cannula.

Arrowe Park Hospital,
Upton, Wirral,
Merseyside L49 5PE

I.E. TWEEDIE

Anaesthesia, 1987, Volume 42, pages 1340–1349

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for August 1987. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Changes in visceral blood flow with elevated intra-abdominal pressure. CALDWELL, C.B., RICOTTA, J.J. *Journal of Surgical Research* 1987; **43:** 14.

Opioid action on the intestine—the importance of the intestinal mucosa. COUPAR, I.M. *Life Sciences* 1987; **41:** 917.

Bradycardia during intra-abdominal surgery—modification by pre-operative anticholinergic agents. COVENTRY, D.M., MEMENEMIN, I., LAWRIE, S. *Anaesthesia* 1987; **42:** 835.

Extrinsic nervous control of motility of small and large intestines and related sphincters. GONELLA, J., BOUVIER, M., BLANQUET, F. *Physiological Reviews* 1987; **67:** 902.

Opioids and opioid receptors in peripheral tissues (irritable bowel syndrome). HEDNER, T., CASSUTO, J. *Scandinavian Journal of Gastroenterology* 1987; **22** (Suppl. 130): 27.

Treatment of postoperative gastrointestinal atony. VERLINDEN, M., MICHIELS, G. *et al. British Journal of Surgery* 1987; **74:** 614.

Pharmacology

Adrenergic drugs and their antagonists

Selective dopamine receptor stimulation in man. CAREY, R.M., HUGHES, J.M. *Clinical and Experimental Hypertension* 1987; **9:** 1009.

Some unconventional control mechanisms in the regulation of the synthesis and metabolism of catecholamines. COMMISSIONG, J.W., SLIMOVITCH, C. In: KAUFMAN, S., ed. *Amino acids in health and disease; new perspectives*. New York: Alan R. Liss, 1987; p. 123.

Nadolol for prevention of variceal rebleeding in cirrhosis: a controlled clinical trial. GATTA, A., MERKEL, C. *et al. Digestion* 1987; **37:** 22.

Effects of physiological increases of plasma noradrenaline on gastric acid secretion and gastrointestinal hormones. GRAFFNER, H., BLOOM, S.R. *et al. Digestive Diseases and Sciences* 1987; **32:** 715.

Pharmacokinetics of long acting propranolol: implications for therapeutic use. NACE, G.S., WOOD, A.J.J. *Clinical Pharmacokinetics* 1987; **13:** 51.

Effect of propranolol on progression of chronic renal disease in partially nephrectomized rats. RADIN, M.J., WILKE, W.L., FETTMAN, M.J. *Research Communications in Chemical Pathology and Pharmacology* 1987; **57:** 3.

Beta-adrenergic receptors and oxygen transport. SUSANNI, E.E.T., MUNDEL, T. *et al. Clinical Physiology and Biochemistry* 1987; **5:** 112.

Effect of beta_1-adrenoceptor blockade on plasma levels of atrial natriuretic peptide during exercise in normal man. THAMSBORG, G., SYKULSKI, R. *et al. Clinical Physiology* 1987; **7:** 313.

Compounds acting on alpha_1- and alpha_2-adrenoreceptors: agonists and antagonists. VIZI, E.S. *Medical Research Reviews* 1986; **6:** 431.

Anaesthetic agents

Changes in breathing pattern and chest wall mechanics after benzodiazepines in combination with meperidine. BERGGREN, L., ERIKSSON, I., MOLLENHOLT, P. *Acta Anaesthesiologica Scandinavica* 1987; **31:** 381.

Assessment of a new hypnotic imidazo-pyridine (zolpidem) as oral premedication. CASHMAN, J.N., POWER, S.J., JONES, R.M. *British Journal of Clinical Pharmacology* 1987; **24:** 85.

The regulation of GABAergic receptors by a novel family of endogenous neuropeptides. COSTA, E., BERKOVICH, A., GUIDOTTI, A. *Life Sciences* 1987; **41:** 799.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MS Dos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Meptazinol overdose producing near fatal respiratory depression. Davison, A.G., Collinson, P.O. *et al. Human Toxicology* 1987; **6:** 331.

Effects of repeated doses of benzodiazepines on arterial blood gases and transcutaneous Po_2. Eriksson, I., Berggren, L. *Acta Anaesthesiologica Scandinavica* 1987; **31:** 357.

Anesthesia and hypertension: the effect of clonidine on perioperative hemodynamics and isoflurane requirements. Ghignone, M., Calvillo, O., Quintin, L. *Anesthesiology* 1987; **67:** 3.

Effects of benzodiazepines on laryngeal reflexes—comparison of lormetazepam and diazemuls. Groves, N.D., Rees, J.L., Rosen, M. *Anaesthesia* 1987; **42:** 808.

Metabolism of chloral hydrate, trichloroethanol and trichloroacetic acid in dogs. Hobara, T., Kobayashi, H. *et al. Pharmacology and Toxicology* 1987; **61:** 58.

Inhibition in the mammalian brain: a new theory of GABA mechanism of action. Hyden, H., Cupello, A. *Acta Physiologica Scandinavica* 1987; **130** (Suppl. 561): 1.

Placental and blood–CSF transfer of orally administered diazepam in the same person. Kanto, J., Scheinin, M. *Pharmacology and Toxicology* 1987; **61:** 72.

Beta endorphin levels in CSF during methadone maintenance. Kosten, T.R., Kreek, M.J. *et al. Life Sciences* 1987; **41:** 1071.

Reversible, narcotic-associated mental status impairment in patients with metastatic cancer. Leipzig, R.M., Goodman, H. *et al. Pharmacology* 1987; **35:** 47.

Theoretical studies of gas mixing and ventilation distribution. Paiva, M., Engel, L.A. *Physiological Reviews* 1987; **67:** 750.

Pharmacokinetic and clinical evaluation of ketamine administered by i.v. and epidural routes. Pedraz, J.L., Lanao, J.M. *et al. International Journal of Clinical Pharmacology, Therapy and Toxicology* 1987; **25:** 77.

Nitrous oxide-induced hypothermia in the rat. Quock, R.M., Panek, R.W. *et al. Life Sciences* 1987; **41:** 683.

Serum fluoride levels in morbidly obese patients: enflurane compared with isoflurane anaesthesia. Strube, P.J., Hulands, G.H., Halsey, M.J. *Anaesthesia* 1987; **42:** 685.

Effects of anaesthetic agents on erythrocyte fragility: comparison of normal and malignant hyperthermia susceptible patients. Tolpin, E.I., Fletcher, J.E. *et al. Canadian Journal of Anaesthesia* 1987; **34:** 366.

Preliminary studies with flunitrazepam, a new intravenous induction agent for anesthesia. Umeh, B.U.O., Iphie, P., Okechukwu, C.C. *Current Therapeutic Research* 1987; **42:** 12.

Halothane hepatotoxicity in glutathione depleted rats. Wilhelm, K.P., Younes, M. *et al. Journal of Applied Toxicology* 1987; **7:** 105.

Analgesic agents

Morphine-induced alterations in plasma and tissue cholesterol levels. Bryant, H.U., Story, J.A., Yim, G.K.W. *Life Sciences* 1987; **41:** 545.

Quaternary naltrexone reveals the central mediation of conditional opioid analgesia. Calcagnetti, D.J., Helmstetter, F.J., Fanslow, M.S. *Pharmacology, Biochemistry and Behavior* 1987; **27:** 529.

Pharmacological properties of a proenkephalin A-derived opioid peptide: BAM 18. Hurlbut, D.E., Evans, C.J. *et al. European Journal of Pharmacology* 1987; **138:** 359.

Transdermal absorption of fentanyl and sufentanil in man. Sebel, P.S., Barrett, C.W. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 529.

Chronic opioid antagonist treatment facilitates nonopioid, stress-induced analgesia. Yoburn, B.C., Truesdell, L.S. *et al. Pharmacology, Biochemistry and Behavior* 1987; **27:** 525.

Muscle relaxants

Malignant hyperthermia susceptibility in neuroleptic malignant syndrome. Caroff, S.N., Rosenberg, H. *et al. Anesthesiology* 1987; **67:** 20.

Cardiovascular, ventilatory and catecholamine responses to maximal dynamic exercise in partially curarized man. Galbo, H., Kjaer, M., Secher, N.H. *Journal of Physiology* 1987; **389:** 557.

Botulinum toxin—structure, action and clinical uses. Hambleton, P., Shone, C.C., Melling, J. In: Jenner, P., ed. *Neurotoxins and their pharmacological implications*. New York: Raven Press, 1987; p. 233.

Induction of hepatic cytochrome P-450c-dependent mono-oxygenase activities by dantrolene in rat. Jayyosi, Z., Totis, M. *et al. Biochemical Pharmacology* 1987; **36:** 2481.

Mechanism for acetylcholine receptor localization at nerve–muscle synapse. Kuromi, H. *Folia Pharmacologica Japonica* 1987; **90:** 73.

Edrophonium provocation test in the diagnosis of diffuse oesophageal spasm. Linsell, J., Owen, W.J. *et al. British Journal of Surgery* 1987; **74:** 688.

Effects of thymectomy in myasthenia gravis. Papatestas, A.E., Genkins, G. *et al. Annals of Surgery* 1987; **206:** 79.

Other drugs

Enzyme induction in humans. Clinical aspects—an overview. Breckenridge, A. *Pharmacology and Therapeutics* 1987; **32:** 95.

Nephrotoxicity of common drugs used in clinical practice. Cooper, K., Bennett, W.M. *Archives of Internal Medicine* 1987; **147:** 1213.

The effect of a single oral dose of ethanol on hepatic blood flow in man. EDWARDS, D.J., BABIAK, L.M., BECKMAN, H.B. *European Journal of Clinical Pharmacology* 1987; **32:** 481.

Guest editorial: the hepatic injury of monoamine oxidase inhibitors. HYMAN, J., ZIMMERMAN, M.D., ISHAK, K.G. *Journal of Clinical Psychopharmacology* 1987; **7:** 211.

Ethanol as a neurotoxin. LEONARD, B.E. *Biochemical Pharmacology* 1987; **36:** 2055.

Ranitidine drug interactions—a literature review. MITCHARD, M., HARRIS, A., MULLINGER, G.M. *Pharmacology and Therapeutics* 1987; **32:** 293.

Age and the metabolism of drugs. RAWLINS, M.D., JAMES, O.F.W. *et al. Quarterly Journal of Medicine* 1987; **64:** 545.

Imipramine blood levels and clinical outcome. RIGAL, J.G., ALBIN, H.CH. *et al. Journal of Clinical Psychopharmacology* 1987; **7:** 222.

Apparatus

Tactile orotracheal tube placement test—a bimanual tactile examination of the positioned orotracheal tube to confirm laryngeal placement. CHARTERS, P., WILKINSON, K. *Anaesthesia* 1987; **42:** 801.

Duplex scanning of the internal carotid artery: an assessment of cerebral blood flow. LEOPOLD, P.W., SHANDALL, A.A. *et al. British Journal of Surgery* 1987; **74:** 630.

Laser Doppler flowmetry, a reliable technique for measuring pharmacologically induced changes in cutaneous blood flow? MULLER, P.H., KELLER, R., IMHOF, P. *Methods and Findings in Experimental and Clinical Pharmacology* 1987; **9:** 409.

Essential monitoring. SYKES, M.K. *British Journal of Anaesthesia* 1987; **59:** 901.

Flammability of endotracheal tube in oxygen and nitrous oxide enriched atmosphere. WOLF, G.L., SIMPSON, J.I. *Anesthesiology* 1987; **67:** 236.

Complications

Cross hepatotoxicity between non-steroidal anti-inflammatory drugs. ANDREJAK, M., DAVION, T. *et al. British Medical Journal* 1987; **295:** 180.

Acute renal failure associated with elevated plasma oncotic pressure. MORAN, M., KAPSNER, C. *New England Journal of Medicine* 1987; **317:** 150.

Obstructive sleep apnea in adults with tonsillar hypertrophy. MOSER, R.J., RAJAGOPAL, K.R. *Archives of Internal Medicine* 1987; **147:** 1265.

Acute myocardial infarction temporally related to cocaine use: clinical, angiographic, and pathophysiologic observations. SMITH, H.W.B., III, LIBERMAN, H.A. *et al. Annals of Internal Medicine* 1987; **107:** 13.

Pitfalls in anaesthetic practice. UTTING, J.E. *British Journal of Anaesthesia* 1987; **59:** 877.

General anaesthetic procedures

Anaesthesia for laparoscopy—a comparison of five techniques including propofol, etomidate, thiopentone and isoflurane. DEGROOD, P.M.R.M., HARBERS, J.B.M. *et al. Anaesthesia* 1987; **42:** 815.

Attenuation of ocular and systemic responses to tracheal intubation by intravenous lignocaine. DRENGER, B., PEER, J. *British Journal of Ophthalmology* 1987; **71:** 546.

Monitoring and analysis of oxygenation and ventilation during rigid bronchoscopic neodymium–YAG laser resection of airway tumors. LENNON, R.L., HOSKING, M.P. *et al. Mayo Clinic Proceeedings* 1987; **62:** 584.

General interest

The pupil. ASHWORTH, B. *Quarterly Journal of Medicine* 1987; **64:** 549.

Low level of superoxide dismutase activity in pheochromocytoma. NAKADA, T., KOIKE, H., KATAYAMA, T. *Journal of Urology* 1987; **138:** 9.

Pathogenesis of post-herpetic neuralgia. SCHON, F., MAYER, M.L., KELLY, J.S. *Lancet* 1987; **2:** 366.

Cardiac pheochromocytoma involving the left main coronary artery presenting with exertional angina. STOWERS, S.A., GILMORE, P. *et al. American Heart Journal* 1987; **114:** 423.

Early surgical history of phaeochromocytoma. WELBOURN, R.B. *British Journal of Surgery* 1987; **74:** 594.

Local analgesia

The effect of changes in arterial CO_2 tension on plasma lidocaine concentration. ALEXANDER, C.M., BERKO, R.S. *et al. Canadian Journal of Anaesthesia* 1987; **34:** 343.

Lidocaine and indocyanine green kinetics—effect of hypoxemia and/or hypercapnia. MARLEAU, S., ONG, H. *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; **242:** 338.

Local anaesthetics inhibit influx of calcium, sodium and potassium into rat ileum, diaphragm and human isolated saphenous vein. WALI, F.A., SUER, A.H. *et al. General Pharmacology* 1987; **18:** 351.

Spinal and epidural analgesia

Epidural anesthesia with bupivacaine: effects of age on neural blockade and pharmacokinetics. VEERING, B.TH., BURM, A.G.L. *et al. Anesthesia and Analgesia* 1987; **66:** 589.

Spinal opioids

Epidural morphine for postoperative pain on medical–surgical wards—a clinical review. BUSCH, E.H., STEDMAN, P.M. *Anesthesiology* 1987; **67:** 101.

Selective agonists for substance P and neurokinin receptors. Drapeau, G., Orleans-Juste, P.D. *et al. Neuropeptides* 1987; **10:** 43.

Systemic methionine-enkephalin evokes cardiostimulatory responses in the human. Giles, T.D., Sander, G.E. *et al. Peptides* 1987; **8:** 609.

Intrathecal administration of a substance-P receptor antagonist—studies on peripheral and CNS hemodynamics and on specificity of action. Helke, C.J., Phillips, E.T., O'Neill, J.T. *Journal of Pharmacology and Experimental Therapeutics* 1987; **242:** 131.

Unexpectedly high levels of opioid peptides in rat brain membranes. Rothman, R.B., Danks, J.A., Iadarola, M.J. *Peptides* 1987; **8:** 645.

Mu-opioid antagonist properties of a cyclic somatostatin octapeptide *in vivo*—identification of mu receptor-related function. Shook, J.E., Pelton, J.T. *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; **242:** 1.

Intrathecal dynorphins suppress hindlimb electromyographic activity in rats. Stevens, C.W., Weinger, M.B., Yaksh, T.L. *European Journal of Pharmacology* 1987; **138:** 299.

Opioid peptides in man—analytical aspects. Terenius, L., Nyberg, F. *Life Sciences* 1987; **41:** 805.

Opioid receptor systems and the endorphins—a review of their spinal organization. Yaksh, T.L. *Journal of Neurosurgery* 1987; **67:** 157.

Obstetric anaesthesia and analgesia

Serum phenytoin during pregnancy, labor and puerperium. Bardy, A.H., Hiilesmaa, V.K., Teramo, K.A.W. *Acta Neurologica Scandinavica* 1987; **75:** 374.

Mechanisms for reduced colloid osmotic pressure in preeclampsia. Bhatia, R.K., Bottoms, S.F. *et al. American Journal of Obstetrics and Gynecology* 1987; **157:** 106.

Anirolac vs. naproxen for postpartum uterine pain. Bloomfield, S.S., Cissell, G.B. *et al. Journal of Pharmacology and Therapeutics* 1987; **42:** 89.

Theory of the etiology of human toxemia of pregnancy: fetal hyperinsulinemia as a compensatory response to decreased uterine blood flow. Bonds, D.R., Crosby, L.O. *Medical Hypotheses* 1987; **23:** 225.

Pregnancy and opiate addiction. Caviston, P. *British Medical Journal* 1987; **295:** 285.

Influence of umbilical vein administration of oxytocin on the third stage of labor: a randomized, double-blind, placebo-controled study. Chestnut, D.H., Wilcox, L.L. *American Journal of Obstetrics and Gynecology* 1987; **157:** 160.

Anaesthetic contribution to maternal mortality. Morgan, M. *British Journal of Anaesthesia* 1987; **59:** 842.

Patient-controlled analgesia with nalbuphine during labor. Podlas, J., Breland, B.D. *Obstetrics and Gynecology* 1987; **70:** 202.

Physiological dead space during general anaesthesia for caesarean section. Shankar, K.B., Moseley, H. *et al. Canadian Journal of Anaesthesia* 1987; **34:** 373.

Paediatric anaesthesia and intensive care

Development of the human coagulation system in the full-term infant. Andrew, M., Paes, B. *et al. Blood* 1987; **70:** 165.

Fetal breathing movements as predictor of favourable pregnancy outcome after oligohydramnios due to membrane rupture in second trimester. Blott, M., Greenough, A. *et al. Lancet* 1987; **2:** 129.

Maternal arterial oxygen saturation during labor and delivery—pain dependent alterations and effects on the newborn. Deckardt, R., Fembacher, P.M. *et al. Obstetrics and Gynecology* 1987; **70:** 21.

High-dose thiopental pharmacokinetics in brain-injured children and neonates. Demarquez, J.L., Galperine, R. *et al. Developmental Pharmacology and Therapeutics* 1987; **10:** 292.

Renal effects of tolazoline in newborn and adult rabbits. Duarte-Silva, M., Naujoks, S., Guignard, J.P. *Developmental Pharmacology and Therapeutics* 1987; **10:** 301.

2nd stage fetal heart rate abnormalities and type of neonatal acidemia. Gilstrap, L.C., Hauth, J.C. *et al. Obstetrics and Gynecology* 1987; **70:** 191.

Abnormalities of lung mechanics in young asthmatic children. Greenough, A., Loftus, B.G. *et al. Thorax* 1987; **42:** 500.

Endotracheal resuscitation of preterm infants at birth. Hoskyns, E.W., Milner, A.D. *et al. Archives of Disease in Childhood* 1987; **62:** 663.

Pulmonary ventilation and gas exchange in children anaesthetized with halothane, enflurane and isoflurane. Johannesson, G.P., Lindahl, S.G.E. *Anesthesiology* 1987; **67:** 375.

Transepidermal water loss during sleep in infants at risk for sudden death. Kahn, A., Vandemerckt, C. *et al. Pediatrics* 1987; **80:** 245.

Effects of heart rate on ventricular size, stroke volume, and output in the normal human fetus: a prospective Doppler echocardiographic study. Kenny, J., Plappert, T. *et al. Circulation* 1987; **76:** 52.

Dexamethasone therapy and cortisol excretion in severe pediatric head injury. Kloti, J., Fanconi, S. *et al. Child's Nervous System* 1987; **3:** 103.

Caudal morphine for postoperative analgesia in children: a comparison with caudal bupivacaine and intravenous morphine. Krane, E.J., Jacobson, L.E. *et al. Anesthesia and Analgesia* 1987; **66:** 647.

Effect of insulin on the distribution of cardiac output in the fetal lamb. Milley, J.R. *Pediatric Research* 1987; **22:** 168.

Oxygen transport and metabolism in the conscious lamb: the effect of hypoxemia. Moss, M., Moreau, G., Lister, G. *Pediatric Research* 1987; **22:** 177.

Early onset of airway reactivity in premature infants with bronchopulmonary dysplasia. Motoyama, E.K., Fort, M.D. *et al. American Review of Respiratory Disease* 1987; **136:** 50.

Changes in arterial blood gases following cardiac asystole during fetal life. Nakamura, K.T., Smith, B.A. *et al. Obstetrics and Gynecology* 1987; **70:** 16.

Effect of cleft palate repair and pharyngeal flap surgery on upper airway obstruction during sleep. Orr, W.C., Levine, N.S., Buchanan, R.T. *Plastic and Reconstructive Surgery* 1987; **80:** 226.

Oral mannitol in control of fluid balance. Poulton, A., Winterborn, M.H. *Archives of Disease in Childhood* 1987; **62:** 729.

Fetal haemodynamics before and after treatment of maternal hypertension in pregnancy. Rasmussen, K. *Danish Medical Bulletin* 1987; **34:** 170.

Cardiac Doppler flows during fetal arrhythmias—physiologic consequences. Reed, K.L., Sahn, D.J. *et al. Obstetrics and Gynecology* 1987; **70:** 1.

Long-term variation in oxygen consumption rate in preterm infants. Roberts, S.B., Murgatroyd, P.R. *et al. Biology of the Neonate* 1987; **52:** 1.

Sleep apnea and vocal cord paralysis secondary to type-1 chiari malformation. Ruff, M.E., Oakes, W.J. *et al. Pediatrics* 1987; **80:** 231.

Hypoglycemia: how little is too much for the embryo? Sadler, T.W., Hunter, E.S., III. *American Journal of Obstetrics and Gynecology* 1987; **157:** 190.

Increased respiratory frequency and variability in high risk babies who die of sudden infant death syndrome. Shannon, D.C., Kelly, D.H. *et al. Pediatric Research* 1987; **22:** 158.

Partial forced expiratory flow–volume curves in young children during ketamine anesthesia. Shulman, D.L., Bar-Yishay, E. *et al. Journal of Applied Physiology* 1987; **63:** 44.

Fetal death following antepartum fetal heart rate testing—a review of 65 cases. Smith, C.V., Nguyen, H.N. *et al. Obstetrics and Gynecology* 1987; **70:** 18.

Cardiorespiratory patterns in siblings of babies with sudden infant death syndrome. Southall, D.P., Alexander, J.R. *et al. Archives of Disease in Childhood* 1987; **62:** 721.

Long-term fate of the diaphragm surgically plicated during infancy and early childhood. Stone, K.S., Brown, J.W. *et al. Annals of Thoracic Surgery* 1987; **44:** 62.

Continuing care for the preterm infant after dismissal from the neonatal intensive care unit. Swanson, J.A., Berseth, C.L. *Mayo Clinic Proceedings* 1987; **62:** 613.

Brain death determination in the newborn. Volpe, J.J. *Pediatrics* 1987; **80:** 293.

Invited review: pathology of the lung in the fetus and neonate, with particular reference to problems of growth and maturation. Wigglesworth, J.S. *Histopathology* 1987; **11:** 671.

Cardiovascular system

Physiology

The relationship of afterload to ejection performance in chronic mitral regurgitation. Corin, W.J., Monrad, E.S. *et al. Circulation* 1987; **76:** 59.

Task Force I: Sudden Cardiac Death. Stress and cardiac arrhythmias. Dimsdale, J.E., Ruberman, W. *et al. Circulation* 1987; **76** (Part 2, Suppl.): I-198.

Subclassification of peripheral dopamine receptors. Hilditch, A., Drew, G.M. *Clinical and Experimental Hypertension* 1987; **9:** 853.

Coronary artery vasodilation in the canine: physiological and pharmacological roles of beta-adrenergic receptors. Jackson, C.V., Pope, T.K., Lucchesi, B.R. *Journal of Cardiovascular Pharmacology* 1987; **10:** 196.

Calcium and regulation of contraction: a short review. Johansson, B. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 1): S9.

Cardiac output by rebreathing in patients with cardiopulmonary diseases. Kallary, M.C., Hyde, R.W. *et al. Journal of Applied Physiology* 1987; **63:** 201.

Review: the coagulation–kinin pathway of human plasma. Kaplan, A.P., Silverberg, M. *Blood* 1987; **70:** 1.

Review article: use of tension measurements to delineate the mode of action of vasodilators. Karaki, H. *Journal of Pharmacological Methods* 1987; **18:** 1.

Relation of sudden death in pure mitral regurgitation, with and without mitral valve prolapse, to repetitive ventricular arrhythmias. Kligfield, P., Hochreiter, C. *et al. American Journal of Cardiology* 1987; **60:** 397.

The molecular pathology of haemophilia. Larner, A.J. *Quarterly Journal of Medicine* 1987; **63:** 473.

Cardiovascular abnormalities accompanying acute spinal cord injury in humans: incidence, time course and severity. Lehmann, K.G., Lane, H.G. *et al. Journal of the American College of Cardiology* 1987; **10:** 46.

Calcium, cell membrane, and excitation–contraction coupling. Lullmann, H., Ziegler, A. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 1): S2.

Methods of measurement of myocardial blood flow in patients: a critical review. Marcus, M.L., Wilson, R.F., White, C.W. *Circulation* 1987; **76:** 245.

The influence of the autonomic nervous system on sudden cardiac death. Schwartz, P.J., De Ferrari, G.M. *Cardiology* 1987; **74:** 297.

Ca-2 channel ligands—comparative pharmacology. SCRIABINE, A. In: VENTER, J.C., TRIGGLE, D., eds. *Structure and physiology of the slow inward calcium channel.* New York: Alan R. Liss, 1987; p. 51.

A dose-responsive model of smoke inhalation injury: severity-related alteration in cardiopulmonary function. SHIMAZU, T., YUKIOKA, T. *et al. Annals of Surgery* 1987; **206:** 89.

Secretion of atrial natriuretic peptide from the heart in man. SINGER, D.R.J., DEAN, J.W. *et al. British Heart Journal* 1987; **58:** 24.

Influence of the sympathetic nervous system and vasopressin on the BP lowering effect of nifedipine in deoxycorticosterone acetate–salt hypertensive rats. TAKATA, Y., YAMASHITA, Y. *et al. Clinical Science* 1987; **73:** 253.

The effect of trauma and surgery on interorgan fluxes of amino acids in man. WERNERMAN, J., VINNARS, E. *Clinical Sciences* 1987; **37:** 129.

Oxygen extraction ratio: a valid indicator of myocardial metabolism in anemia. WILKERSON, D.K., ROSEN, A.L. *et al. Journal of Surgical Research* 1987; **42:** 629.

A new unstable and low oxygen affinity hemoglobin variant: Hb J-Auckland. WILLIAMSON, D., WELLS, R.M. *et al. Hemoglobin* 1987; **11:** 221.

Atrial natriuretic peptide secretion in mitral stenosis. YOSHIMI, H., INOUE, I. *et al. American Journal of Cardiology* 1987; **60:** 396.

Task Force 2: Sudden Cardiac Death. Neural–cardiac interactions. ZIPES, D.P., LEVY, M.N. *et al. Circulation* 1987; **76** (Part 2, Suppl.): I-202.

Treatment and medication

The proarrhythmic effects of antiarrhythmic drugs. CREAMER, J.E., NATHAN, A.W., CAMM, A.J. *American Heart Journal* 1987; **114:** 397.

Development of congestive heart failure and alterations in LV function in patients with sustained ventricular tachyarrhythmias treated with amiodarone. DE PAOLA, A.A.V., HOROWITZ, L.N. *et al. American Journal of Cardiology* 1987; **60:** 276.

Unreliability of hemodynamic indexes of left ventricular size during cardiac surgery. DOUGLAS, P.S., EDMUNDS, L.H. *et al. Annals of Thoracic Surgery* 1987; **44:** 31.

Responses to mental stress and physical provocations before and during long term treatment of hypertensive patients with beta-blockers/hydrochlorothiazide. ELIASSON, K., KAHAN, T. *et al. British Journal of Clinical Pharmacology* 1987; **24:** 1.

Cardiovascular effects of doxepin in cardiac patients with ventricular arrhythmias. GIARDINA, E.-G.V., COOPER, T.B. *et al. Clinical Pharmacology and Therapeutics* 1987; **42:** 20.

New inotropic drugs for heart failure. GOLDERBERG, I.F., COHN, J.N. *Journal of the American Medical Association* 1987; **258:** 493.

Routine use of beta-blockers following myocardial infarction: a note of dissent. GREENBAUM, R.A. *Journal of the Royal Society of Medicine* 1987; **80:** 402.

Experience with nalbuphine, a new opioid analgesic, in acute myocardial infarction. GREENBAUM, R.A., KAYE, G., MASON, P.D. *Journal of the Royal Society of Medicine* 1987; **80:** 418.

Management of shock in acute myocardial infarction: changing concepts; past, present and future. HAGER, W.D., KATZ, A.M. *Cardiology* 1987; **74:** 286.

Hemodynamic and pharmacokinetic aspects of the interactions between verapamil and pindolol. HAMANN, S.R., KALTENBORN, K.E., MCALLISTER, R.G., JR. *Pharmacology* 1987; **34:** 326.

Nifedipine–propranolol interaction: dependence of cardiovascular effects on plasma drug concentrations. HAMANN, S.R., KALTENBORN, K.E., MCALLISTER, R.G., JR. *Journal of Cardiovascular Pharmacology* 1987; **10:** 182.

Predictors of antiarrhythmic drug efficacy in patients with malignant ventricular tachyarrhythmias. HOHNLOSER, S.H., RAEDER, E.A. *et al. American Heart Journal* 1987; **114** (Part I): 1.

The comparative effects of verapamil and a new dihydropyridine calcium channel blocker on digoxin pharmacokinetics. JOHNSON, B.F., WILSON, J. *et al. Clinical Pharmacology and Therapeutics* 1987; **42:** 66.

Effect of diltiazem and propranolol on myocardial ischaemia during unrestricted daily life in patients with effort-induced chronic stable angina pectoris. KHURMI, N.S., OHARA, M.J. *et al. European Journal of Clinical Pharmacology* 1987; **32:** 443.

Effects of intravenous S-9780, an angiotensin-converting enzyme inhibitor, in normotensive subjects. LEES, K.R., REID, J.L. *Journal of Cardiovascular Pharmacology* 1987; **10:** 129.

Functional antagonism of noradrenaline responses by felodipine and other calcium antagonists in vascular smooth muscles. LJUNG, B., KJELLSTEDT, A. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 1): S82.

Management of ventricular tachycardia. MORADY, F. *Chest* 1987; **92:** 157.

Hypertonic saline resuscitates dogs in endotoxin shock. MULLINS, R.J., HUDGENS, R.W. *Journal of Surgical Research* 1987; **43:** 37.

Effects of felodipine on local and neurogenic control of vascular resistance. NORDLANDER, M., THALEN, P. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 1): S100.

A comparison of the cardioselectivity of five beta-adrenoceptor blocking drugs. PRINGLE, T.H., RIDDELL, J.G., SHANKS, R.G. *Journal of Cardiovascular Pharmacology* 1987; **10:** 228.

Nicardipine for systemic hypertension: effects on blood pressure and target organ function. RAM, C.V.S. *American Journal of Cardiology* 1987; **59:** 251.

Resuscitation in haemorrhagic shock—pulmonary and renal effects: an adverse effect of stabilised plasma protein solution on renal function? RAMSAY, G., LEDINGHAM, I.MCA. *Circulatory Shock* 1987; **22:** 261.

Effect of food on nifedipine pharmacokinetics. REITBERG, D.P., LOVE, S.J. *et al. Clinical Pharmacology and Therapeutics* 1987; **42:** 72.

The pharmacokinetics and pharmacodynamics of newer inotropic agents. ROCCI, M.L., JR., WILSON, H. *Clinical Pharmacokinetics* 1987; **13:** 91.

Primary ventricular fibrillation. RUSKIN, J.N. *New England Journal of Medicine* 1987; **317:** 307.

Clinical application of atrial natriuretic polypeptide in patients with congestive heart failure: beneficial effects on left ventricular function. SAITO, Y., NAKAO, K. *et al. Circulation* 1987; **76:** 115.

Sotalol: a beta blocker with unique antiarrhythmic properties. SINGH, B.N., NADEMANEE, K. *American Heart Journal* 1987; **114** (Part I): 121.

Evidence for an antagonism between caffeine and adenosine in the human cardiovascular system. SMITS, P., BOEKEMA, P. *et al. Journal of Cardiovascular Pharmacology* 1987; **10:** 136.

Activity-mode cardiac pacing; clinical considerations. TILBURY, R.T., VLIETSTRA, R.E., HAYES, D.L. *Mayo Clinic Proceedings* 1987; **62:** 607.

Immediate effects of bumetanide on systemic haemodynamics and left ventricular volume in acute and chronic heart failure. VERMA, S.P., SILKE, B. *et al. British Journal of Clinical Pharmacology* 1987; **24:** 21.

New thrombolytic drugs in acute myocardial infarction: theoretical and practical considerations. VERSTRAETE, M. *Circulation* 1987; **76** (Suppl.): II-31.

Surgical revascularization of acute evolving MI without blood cardioplegia fails to restore postischemic function in the involved segment. VINTEN-JOHANSEN, J., FAUST, K.B. *et al. Annals of Thoracic Surgery* 1987; **44:** 66.

In-hospital prognosis of patients with acute myocardial infarction complicated by primary ventricular fibrillation. VOLPI, A., MAGGIONI, A. *et al. New England Journal of Medicine* 1987; **317:** 257.

Reduction in sudden death and total mortality by antiarrhythmic therapy evaluated by electrophysiologic drug testing. WALLER, T.J., KAY, H.R. *et al. Journal of the American College of Cardiology* 1987; **10:** 83.

Animal pharmacology of nicardipine and its clinical relevance. WHITING, R.L. *American Journal of Cardiology* 1987; **59:** 31.

Angiotensin-converting enzyme inhibitors in essential hypertension. ZANCHETTI, A. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 3): S2.

Mechanical assistance for cardiogenic shock following cardiac surgery, myocardial infarction, and cardiac transplantation. ZUMBRO, G.L., KITCHENS, W.R. *et al. Annals of Thoracic Surgery* 1987; **44:** 11.

Respiration

Physiology

Changes in cardiac output during sustained maximal ventilation in humans. ANHOLM, J.D., JOHNSON, R.L., RAMANATHAN, M. *Journal of Applied Physiology* 1987; **63:** 181.

Breathlessness and respiratory mechanics during reflex or voluntary hyperventilation in patients with chronic airflow limitation. FREEDMAN, S., LANE, R., GUZ, A. *Clinical Science* 1987; **73:** 311.

Oxygenation and breathing pattern during phasic and tonic REM in patients with chronic obstructive pulmonary disease. GEORGE, C.F., WEST, P., KRYGER, M.H. *Sleep* 1987; **10:** 234.

Oxygen diffusing capacity estimates derived from measured VA/Q distributions in man. HAMMOND, M.D., HEMPLEMAN, S.C. *Respiration Physiology* 1987; **69:** 129.

Ventilatory responses to inhaled carbon dioxide at rest and during exercise in man. JACOBI, M.S., IYAWE, V.I. *et al. Clinical Sciences* 1987; **73:** 177.

Airway caliber and the work of breathing in humans. JENNINGS, S.J., WARREN, J.B., PRIDE, N.B. *Journal of Applied Physiology* 1987; **63:** 20.

Hemoglobin autoxidation at physiological concentrations. MANSOURI, A., PERRY, C.A. *Hemoglobin* 1987; **11:** 353.

The labile respiratory activity of ribcage muscles of the rat during sleep. MEGIRIAN, D., POLLARD, M.J., SHERREY, J.H. *Journal of Physiology* 1987; **389:** 99.

Respiratory airflow pattern in patients with chronic airway obstruction. MINETTI, A.E., BRAMBILLA, I., LAPORTUNA, C.L. *Clinical Physiology* 1987; **7:** 283.

Effects of theophylline and enprofylline on diaphragmatic contractility. MURCIANO, D., AUBIER, M. *et al. Journal of Applied Physiology* 1987; **63:** 51.

Ventilation during carbon dioxide loading in anaesthetized women. MYATT, J.K., WOLFF, C.B. *Bulletin Europeen de Physiopathologie Respiratoire* 1987; **23:** 113.

Hypercapnia and sleep O_2 desaturation in chronic obstructive pulmonary disease. PEREZ-PADILLA, R., CONWAY, W. *et al. Sleep* 1987; **10:** 216.

Influence of upper airway sensory receptors on respiratory muscle activation in humans. REDLINE, S., STROHL, K.P. *Journal of Applied Physiology* 1987; **63:** 368.

Effects of carbon dioxide on mental performance. SAYERS, J.A., SMITH, R.E.A. *et al. Journal of Applied Physiology* 1987; **63:** 25.

Detection of hypercapnia by normal subjects.

Schwartzstein, R.M., La Hive, K. *et al. Clinical Science* 1987; **73:** 333.

Cold facial stimulation reduces breathlessness induced in normal subjects. Schwartzstein, R.M., La Hive, K. *et al. American Review of Respiratory Disease* 1987; **136:** 58.

Orthodeoxia—a new finding in interstitial fibrosis. Tenholder, M.F., Russell, M.D. *et al. American Review of Respiratory Disease* 1987; **136:** 161.

Short term variability in FEV$_1$, and bronchodilator responsiveness in patients with obstructive ventilatory defects. Tweeddale, P.M., Alexander, F., McHardy, G.J.R. *Thorax* 1987; **42:** 487.

Qualification of regional ventilation in humans using a short-lived radiotracer—theoretical evaluation of the steady-state model. Valind, S.O., Rhodes, C., Jonson, B. *Journal of Nuclear Medicine* 1987; **28:** 1144.

A non-invasive method for measuring inspiratory muscle fatigue during progressive isocapnic hyperventilation in man. Vilozni, D., Baryishay, E. *et al. European Journal of Applied Physiology* 1987; **56:** 433.

Airway involvement in ulcerative colitis. Wilcox, P., Miller, R. *et al. Chest* 1987; **92:** 18.

Effects of reduced frequency breathing on arterial hypoxemia during exercise. Yamamoto, Y., Mutoh, Y. *et al. European Journal of Applied Physiology and Occupational Physiology* 1987; **56:** 522.

Treatment and medication

Effect of theophylline on diaphragmatic muscle function. Aubier, M. *Chest* 1987; **92** (Suppl): 27S.

The effects of vasodilation with prostacyclin on oxygen delivery and uptake in critically ill patients. Bihari, D., Smithies, M. *et al. New England Journal of Medicine* 1987; **317:** 397.

The effect of nitroprusside on pulmonary edema, oxygen exchange, and blood flow in hydrochloric acid aspiration. Gottlieb, S.S., Wood, L.D.H. *et al. Anesthesiology* 1987; **67:** 203.

The difficult pneumothorax. Harvey, J.E., Jeyasingham, K. *British Journal of Diseases of the Chest* 1987; **81:** 209.

Theophylline as a bronchodilator in COPD and its combination with inhaled beta-adrenergic drugs. Jenne, J.W. *Chest* 1987; **92** (Suppl.): 7S.

Continuous positive airway pressure effect on functional residual capacity, vital capacity and its subdivisions. Lindner, K.H., Lotz, P., Ahnefeld, F.W. *Chest* 1987; **92:** 66.

Post-mortem concentrations of salbutamol, terbutaline and theophylline in asthma patients. Lindsjo, M., Boman, G. *et al. European Journal of Respiratory Diseases* 1987; **71:** 2.

The role of theophylline in the treatment of dyspnea in COPD. Mahler, D.A. *Chest* 1987; **92** (Suppl): 2S.

Role of bronchoalveolar lavage in the assessment of opportunistic pulmonary infections: utility and complications. Martin, W.J., II, Smith, T.F. *et al. Mayo Clinic Proceedings* 1987; **62:** 549.

The effects of indomethacin on edema and gas exchange in canine acid aspiration. Mayers, I., Breen, P.H. *et al. Respiration Physiology* 1987; **69:** 149.

Pulmonary vasodilator therapy for chronic obstructive pulmonary disease and cor pulmonale. Morley, T.F., Zappasodi, S.J. *et al. Chest* 1987; **92:** 71.

Effects of removing oxygen from patients with chronic obstructive pulmonary disease. Selinger, S.R., Kennedy, T.P. *et al. American Review of Respiratory Disease* 1987; **136:** 85.

Central nervous system

Physiology

Plasma and cerebrospinal fluid nucleosides and oxypurines in acute liver failure. Berlinger, W.G., Stene, R.A. *et al. Journal of Laboratory and Clinical Medicine* 1987; **110:** 137.

Neurotoxins and the selective vulnerability of brain. Collins, R.C. In: Jenner, P., ed. *Neurotoxins and their pharmacological implications.* New York: Raven Press, 1987; p. 1.

Hyperglycemia, cerebrospinal fluid lactic acidosis, and cerebral blood flow in severely head-injured patients. De Salles, A.A.F., Muizelaar, J.P., Young, H.F. *Neurosurgery* 1987; **21:** 45.

The role of the brain stem in generalized epileptic seizures. Faingold, C.L. *Metabolic Brain Disease* 1987; **2:** 81.

Neuropsychological dysfunction in sleep apnea. Greenberg, G.D., Watson, R.K., Deptula, D. *Sleep* 1987; **10:** 254.

Brain cellular and mitochondrial respiration in media of altered pH. Holtzman, D., Olson, J.E. *et al. Metabolic Brain Disease* 1987; **2:** 127.

Metabolic and clinical correlates of acute ischemic infarction. Kusner, M., Reivich, M. *et al. Neurology* 1987; **37:** 1103.

Neural control of internal anal sphincter function. Lubowski, D.Z., Nicholls, R.J. *et al. British Journal of Surgery* 1987; **74:** 668.

Microcirculation and neurotransmitter metabolism in the pathophysiology of brain ischaemia: a role for calcium. Magnoni, M.S., Govoni, S., Trabucchi, M. *Drugs* 1987; **33** (Suppl. 2): 12.

Neurotransmitters and psychosis. Owen, F., Crow, T.J. *British Medical Bulletin* 1987; **43:** 651.

Effects of psychotropic drugs on neurotransmitters in man. Potter, W.Z., Rudorfer, M.V. *et al. Life Sciences* 1987; **41:** 817.

Peptides and central neural regulation of the circulation. Reid, J.L., Rubin, P.C. *Physiological Reviews* 1987; **67:** 725.

State-of-the-art review: sleep research in affective illness: state of the art circa 1987. Reynolds, C.F., III, Kupfer, D.J. *Sleep* 1987; **10:** 199.

Minireview: multiple mechanisms of serotonergic signal transduction. Roth, B.L., Chuang, D.M. *Life Sciences* 1987; **41:** 1051.

Treatment and medication

Drugs for the treatment of traumatic brain injury. Cragoe, E.J., Jr. *Medical Research Reviews* 1987; **7:** 271.

The therapeutic value of nimodipine in experimental focal cerebral ischemia—neurological outcome and histopathological findings. Germano, I.M., Bartkowski, H.M. *et al. Journal of Neurosurgery* 1987; **67:** 81.

Clinical pharmacokinetic considerations in the treatment of increased intracranial pressure. Heinemeyer, G. *Clinical Pharmacokinetics* 1987; **13:** 1.

Nerve regeneration and repair. Lundborg, G. *Acta Orthopaedica Scandinavica* 1987; **58:** 145.

Neurologic and neuropsychological morbidity following major surgery—comparison of coronary artery bypass and peripheral vascular surgery. Shaw, P.J., Bates, D. *et al. Stroke* 1987; **18:** 700.

Endocrine and metabolic

Physiology

Insulin suppresses its own secretion *in vivo*. Argoud, G.M., Schade, D.S., Eaton, R.P. *Diabetes* 1987; **36:** 959.

The metabolic cost of fever. Baracos, V.E., Whitmore, W.T., Gale, R. *Canadian Journal of Physiology and Pharmacology* 1987; **65:** 1248.

Abnormal diurnal urinary sodium and water excretion in diabetic autonomic neuropathy. Bell, G.M., Reid, W. *et al. Clinical Science* 1987; **73:** 259.

Reactive hypoglycaemia. Betteridge, D.J. *British Medical Journal* 1987; **295:** 286.

Regular review: somatostatin. Bloom, S.R., Polak, J.M. *British Medical Journal* 1987; **295:** 288.

Fluid–electrolyte shift and renin–aldosterone responses to exercise under hypoxia. Bouissou, P., Peronnet, F. *et al. Hormone and Metabolic Research* 1987; **19:** 331.

Ammonia: key factor in the pathogenesis of hepatic encephalopathy. Butterworth, R.F., Giguere, J.F. *et al. Neurochemical Pathology* 1987; **6:** 1.

The complement system in type-1 (insulin dependent) diabetes. Charlesworth, J.A., Timmermans, V. *et al. Diabetologia* 1987; **30:** 372.

Hormonal responses to graded surgical stress. Chernow, B., Alexander, H.R. *et al. Archives of Internal Medicine* 1987; **147:** 1273.

Naloxone decreases the inhibiting effect of ethanol on the release of arginine–vasopressin induced by cigarette smoking in man. Chiodera, P., D'Amato, L. *et al. Metabolism* 1987; **36:** 804.

Effect of obesity and weight loss on the arginine–vasopressin response to insulin-induced hypoglycaemia. Coiro, V., Chiodera, P. *Clinical Endocrinology* 1987; **27:** 253.

Effectiveness of vasopressin regulation of coronary blood flow in congestive heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Crozier, I.G., Ikram, H. *et al. American Journal of Cardiology* 1987; **60:** 390.

Potentiated hormonal responses in a model of traumatic injury. Demaria, E.J., Lilly, M.P., Gann, D.S. *Journal of Surgical Research* 1987; **43:** 45.

New findings in apparent mineralocorticosteroid excess. Dimartino-Nardi, J., Stoner, E. *et al. Clinical Endocrinology* 1987; **27:** 49.

Insulin resistance in essential hypertension. Ferrannini, E., Buzzigoli, G. *et al. New England Journal of Medicine* 1987; **317:** 350.

Effect of physiologic hyperinsulinemia on skeletal muscle protein synthesis and breakdown in man. Gelfand, R.A., Barrett, E.J. *Journal of Clinical Investigation* 1987; **80:** 1.

Influence of sympathetic nervous system on hypoglycaemic warning symptoms. Heller, S.R., MacDonald, I.A. *et al. Lancet* 1987; **2:** 359.

Metabolic and cardiovascular responses to epinephrine in diabetic autonomic neuropathy. Hilsted, J., Richter, E. *et al. New England Journal of Medicine* 1987; **317:** 421.

Vasopressin antagonists—present and future. Hofbauer, K.G., Mah, S.C. *Kidney International* 1987; **32** (Suppl. 21): S76.

The renal concentrating mechanism. Jamison, R.J. *Kidney International* 1987; **32** (Suppl. 21): S43.

Effects of highly potent octapeptide analogs of somatostatin on growth hormone, insulin and glucagon release. Karashima, T., Cai, R.Z., Schally, A.V. *Life Sciences* 1987; **41:** 1011.

Role of alpha$_2$-adrenergic receptor in platelet activation during insulin-induced hypoglycemia in normal subjects. Kishikawa, H., Takeda, H. *et al. Diabetes* 1987; **36:** 407.

Significance of blood lactate levels in critically ill patients with liver disease. Kruse, J.A., Zaidi, S.A.J., Carlson, R.W. *American Journal of Medicine* 1987; **83:** 77.

Liver function abnormalities in chronic heart failure—influence of systemic hemodynamics. Kubo, S.H., Walter, B.A. *et al. Archives of Internal Medicine* 1987; **147:** 1227.

Awareness of hypoglycaemia in diabetes. Leading Article. *Lancet* 1987; **2:** 371.

Controversies in lactic acidosis. Mizock, B.A. *Journal of the American Medical Association* 1987; **258:** 497.

Stress, prolactin and hypothalamic dopaminergic neurons. Moore, K.E., Demarest, K.T., Lookingland, K.J. *Neuropharmacology* 1987; **26:** 801.

Neural control of somatotropic function. Muller, E.E. *Physiological Reviews* 1987; **67:** 962.

Vasopressin and fever: evidence supporting the existence of an endogenous antipyretic system in the brain. Naylor, A.M., Cooper, K.E., Veale, W.I. *Canadian Journal of Physiology and Pharmacology* 1987; **65:** 1333.

Neuroendocrine control of vasopressin secretion and its effect on blood pressure in subjects with spinal cord transection. Poole, C.J.M., Williams, T.D.M. *et al. Brain* 1987; **110** (Part 3): 727.

Basic research of hypothalamic–pituitary–adrenal neuroendocrinology—an overview of the physiological function of the stress response. Reichlin, S. In: Halbreich, U., ed. *Hormones and depression.* New York: Raven Press, 1987; p. 21.

Effects of lithium on the endocrine system: a review. Salata, R., Klein, I. *Journal of Laboratory and Clinical Medicine* 1987; **110:** 130.

Diabetes mellitus and thermoregulation. Scott, A.R., Bennett, T., MacDonald, I.A. *Canadian Journal of Physiology and Pharmacology* 1987; **65:** 1365.

Neurohypophyseal peptide function during early postoperative diabetes insipidus. Seckl, J.R., Dunger, D.B., Lightman, S.L. *Brain* 1987; **110** (Part 3): 737.

The influence of anaesthesia on the acute phase protein response to surgery. Simpson, P.J., Radford, S.G., Lockyer, J.A. *Anaesthesia* 1987; **42:** 690.

Plasma renin system during exercise in normal men. Staessen, J., Fagard, R. *et al. Journal of Applied Physiology* 1987; **63:** 188.

Hypoglycaemia unawareness in diabetics transferred from beef/porcine insulin to human insulin. Teuscher, A., Berger, W.G. *Lancet* 1987; **2:** 382.

Possible mechanism for cerebral oedema in diabetic ketoacidosis. Van der Meulen, J.A., Klip, A., Grinstein, S. *Lancet* 1987; **2:** 306.

The natriuretic effect of an acute peroral load of potassium chloride after inhibition of potassium secretion with amiloride or lithium. Vendelin, O.O., Thomsen, K. *Pharmacology and Toxicology* 1987; **61:** 9.

Importance of substrate competition in the mechanism of insulin resistance in man. Vouillamoz, D., Temler, E. *et al. Metabolism* 1987; **36:** 715.

Effect of severe burn injury on substrate cycling by glucose and fatty acids. Wolfe, R.R., Herndon, D.N. *et al. New England Journal of Medicine* 1987; **317:** 403.

Hyperglycemia decreases glucose uptake in type I diabetes. Yki-Jarvinen, H., Helve, E., Koivisto, V.A. *Diabetes* 1987; **36:** 892.

Treatment and medication

Suppression of plasma renin activity by cyclosporine. Bantle, J.P., Boudreau, R.J., Ferris, T.F. *American Journal of Medicine* 1987; **83:** 59.

Prevention of ischaemic acute renal failure with superoxide dismutase and sucrose. Bayati, A., Hellberg, O. *et al. Acta Physiologica Scandinavica* 1987; **130:** 367.

Renal effects of converting enzyme inhibition. Brunner, H.R., Waeber, B., Nussberger, J. *Journal of Cardiovascular Pharmacology* 1987; **9** (Suppl. 3): S6.

Short-term metabolic effects of recombinant human insulin-like growth factor I in healthy adults. Guler, H.-P., Zapf, J., Froesch, E.R. *New England Journal of Medicine* 1987; **317:** 137.

Hypotensive and sedative effects of insulin in autonomic failure. Mathias, C.J., Da Costa, D.F. *et al. British Medical Journal* 1987; **295:** 161.

Preoperative insulin reverses cachexia and decreases mortality in tumor-bearing rats. Moley, J.F., Morrison, S.D., Norton, J.A. *Journal of Surgical Research* 1987; **43:** 21.

The effect of corticosteroids on postoperative edema. Nordstrom, R.E., Nordstrom, R. *Plastic and Reconstructive Surgery* 1987; **80:** 85.

Glucose: a re-evaluation of its intraoperative use. Sieber, F.E., Smith, D.S. *et al. Anesthesiology* 1987; **67:** 72.

Lithium inhibits the action of fludrocortisone on the kidney. Stewart, P.M., Grieve, J. *et al. Clinical Endocrinology* 1987; **27:** 63.

Pain

Treatment and medication

Incidence and characteristics of pain in a sample of medical–surgical inpatients. Donovan, M., Dillon, P., McGuire, L. *Pain* 1987; **30:** 69.

Tricyclic antidepressants in the treatment of cancer pain: a review. Magni, G., Conlon, P., Arsie, D. *Pharmacopsychiatry* 1987; **20:** 160.

Other

Physiology

Minireview: neuropeptides: conductors of the immune orchestra. Morley, J.E., Kay, N.E. *et al. Life Sciences* 1987; **41:** 527.

Anaesthesia, 1987, Volume 42, page 1350

Stop Press

Courses in Anaesthesia

FFARCS Part 2

LONDON

Department of Anaesthetics, St. Thomas' Hospital, London SE1 7EH.	Day release, Fridays, 5 February– 15 April 1988	£120	Anaesthetic Course Secretary, Department of Anaesthetics, St. Thomas' Hospital, Lambeth Palace Road, London SE1 7EH.

FFARCS Part 3

EDINBURGH

	September 1987/January 1988 and February/June 1988. In-service courses for junior hospital doctors, Monday afternoons		The Post-Graduate Dean, Edinburgh Post-Graduate Board for Medicine, Pfizer Foundation, Hill Square, Edinburgh EH8 9DR.

Anaesthesia, 1987, Volume 42, pages 1351–1400

Author Index, Volume 42 (1987)

c = correspondence; f = forum

ABBOTT, M. A. & SAMUEL, J. R. The control of intra-ocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique, 1008 (f)
ADAMS, A. K. Early retirement and morbidity, 1024 (c)
ADDICOTT, L. S. *see* KNIGHT, B. H.
ADURO-DOMINAH, A. *see* BYRNE, F.
AITKENHEAD, A. R. Clinical investigations—why we must keep control: editorial, 583
ALDERSON, J. D. Cardiovascular collapse following epidural anaesthesia for Caesarean section in a patient with aortic incompetence, 643
ALDERSON, J. D. Cardiovascular collapse following epidural anaesthesia for Caesarean section: a reply, 1230 (c)
ALDRIDGE, L. M. An unusual cause of upper airways obstruction, 1239 (c)
ALDRIDGE, L. M. Postoperative complications of dystrophia myotonica, 1121 (c)
ALLEN, P. & WREN, W. S. Sampling for carbon dioxide, 560 (c)
ALLEN, S. C., BARR, A. M., BROCK, P. J., HALL, R. M., JAGO, R. H., MCWILLIAMS, D. M., SMITH, T. G. C., WALDMANN, C. S., YOUNG, E. & RIMMER, M. E. A matter of vigilance, 434 (c)
ALLISON, A. *see* SMITH, B. E.
ALLSOP, P. & TWIGLEY, A. J. The neuroleptic malignant syndrome. Case report with a review of the literature, 49
ALLT-GRAHAM, J., GALLAGHER, J. & STRANGEWAYS, J. E. M. Humidification by filters: a reply, 1119 (c)
ALLT-GRAHAM, J. *see* GALLAGHER, J.
ALSTON, R. P. Expiratory obstruction in a circle system, 1120 (c)
ALSTON, R. P. & OATES, P. D. Cardiac output during an anaphylactoid reaction, 892 (c)
APADOO, A. *see* SPARGO, P. M.
ARCHER, P. L. *see* SPRAGUE, N. B.
ARTRU, A. A. *see* POWERS, K. M.
ASHBY, M. W. *see* SINCLAIR, M. E.
AVELING, W. *see* RUTTER, G. G. R.
AVELING, W. *see* SHERRY, K. M.

BACH, A. B. *see* JACOBSEN, J.
BALMER, H. G. R. *see* GAYLARD, D. G.
BAMBER, P. A. Possible safety hazard on anaesthetic machines, 782 (c)
BAMBER, P. A. *see* HOWELL, P. J.
BARAKA, A., MOGHRABI, R. & YAZIGI, A. Unilateral pulmonary oedema/atelectasis in the lateral decubitus position, 171
BARBER, J. D. *see* GREBENIK, C. R.
BARKER, I. *see* REID, M. F.
BARNES, P. K. *see* ROE, P. G.
BARR, A. M. *see* ALLEN, S. C.
BARRETT, R. F. *see* CROSS, G. D.
BARROWCLIFFE, M. P. Spurious central venous pressure, 293
BASKETT, P. J. F. Professor John Clutton-Brock, MA, MB, BChir, FFARCS, DA, 1912–1986, 426 (c)
BATEMAN, P. E. *see* PARK, G. R.
BATRA, Y. K. *see* PURI, G. D.
BEAUMONT, A. *see* EASON, J. R.
BEGON, C. *see* BRASSEUR, L.
BELL, B. *see* BROWN, T. C. K.
BEMBRIDGE, J. L. *see* SUGDEN, J. C.
BEMBRIDGE, M. An inflatable paediatric wedge, 213 (c)
BENNETT, A. J. Peri-operative fluids, 570 (c)
BENNETT, N. R. *see* REID, M. F.
BETHUNE, D. *see* BODENHAM, A.
BETHUNE, D. W. Pre-operative visits, 553 (c)
BETHUNE, D. W. *see* KIPLING, R. M.
BICKFORD-SMITH, P. & EVANS, C. S. Error in labelling, 572 (c)
BIRNIE, R. *see* BLOM, H. J.

BLACKBURN, C. Respiratory arrest after epidural sufentanil, 665 (c)
BLAKE, D. *see* GRIFFITHS, R. B.
BLAKELEY, C. R. A way forward for intensive care, 552 (c)
BLANC, V. F. Ventilation and the oculocardiac reflex, 324 (c)
BLANCO, E. *see* SOLARES, G.
BLISS, J. M. *see* HANKS, G. W.
BLOGG, C. E. *see* TIPPING, T.
BLOGG, C. E. *see* WAIT, C. M.
BLOM, H. J., KARSDORP, V., BIRNIE, R. & DAVIES, G. Phaeochromocytoma as a cause of pulmonary oedema, 646
BLOOR, G. K., JONES, M. J. & TURNER, D. A. B. Absence of clinically significant neonatal respiratory depression after prolonged maternal propofol administration, 1233 (c)
BLYTH, A. *see* HODSMAN, N. B. A.
BODENHAM, A., LATIMER, R. & BETHUNE, D. Respiratory obstruction following vocal cord injection. A complication on induction of anaesthesia, 289
BOLD, A. M. *see* WARRAN, P.
BONE, M. E., GALLER, D. & FLYNN, P. J. Arterial oxygen saturation during general anaesthesia for paediatric dental extractions, 879 (f)
BOOKER, P. D. Postoperative analgesia for neonates: editorial, 343
BOOKER, P. D. *see* GODDARD, J. M.
BOURA, J. *see* BRASSEUR, L.
BOURKE, D. L. Morphine-induced respiratory depression in the elderly, 428 (c)
BOVE, M. *see* WANG, L. P.
BOWEN, D. J., DAYKIN, A. P., SAUNDERS, D. A. & NORMAN, J. Morphine-induced respiratory depression in the elderly: a reply, 428 (c)
BOYKETT, M. Minitracheostomy, 87 (c)
BRADSHAW, E. G. *see* RAYBOULD, D.
BRAIN, A. I. J. The cricoid yoke, 780 (c)
BRANTHWAITE, M. A way forward for intensive care, 550 (c)
BRASSEUR, L., BOURA, J., BRUNET, A.-M., GABRIEL, P., BEGON, C. & DESCORPS-DECLERE, A. Failure of long-term epidural catheters, 557 (c)
BRAUDE, N. Unstable cervical fracture, 1334 (c)
BRAY, B. M. Risk of infection from water bath blood warmers, 778 (c)
BRAY, B. M., JONES, H. M. & GRUNDY, E. M. Tracheal versus intravenous atropine. A comparison of the effects on heart rate, 1188
BRICKER, S. R. W. & RAITT, D. G. Angioneurotic oedema following etomidate/lignocaine, 323 (c)
BRIGHOUSE, D. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1226 (c)
BROCK, P. J. *see* ALLEN, S. C.
BROCKWAY, M. S. *see* DUNDAS, C. R.
BRODRICK, P. M. *see* WAINWRIGHT, A. P.
BROMAGE, P. R. *see* WÜST, H. J.
BROMLEY, L. *see* WITHINGTON, D. E.
BROWN, T. C. K., GREGORY, M., BELL, B. & CAMPBELL, P. C. Liver tumours and muscle relaxants. Electromyographic studies in children, 1284
BROWNE, D. R. G. A way forward for intensive care, 550 (c)
BRUNET, A.-M. *see* BRASSEUR, L.
BRYSON, T. H. L. *see* RUSSELL, G. N.
BUCKLEY, P. M. & BUSH, G. H. Difficulty in extubation, 778 (c)
BULLINGHAM, R. E. S. *see* GILLIES, G. W. A.
BURGESS, R. & WROBEL, J. Shelf-life of sodium citrate (0.3M), 1019 (c)
BURNS, J. *see* HODSMAN, N. B. A.
BURNS, T. H. S. Unexplained hepatitis following halothane, 76 (c)
BUSH, G. H. *see* BUCKLEY, P. M.
BUSH, G. H. *see* SAPSFORD, D. J.
BUSH, G. H. *see* UNDERHILL, S.
BUTCHERS, J. The severance of epidural catheters, 315 (c)
BYERS, G. F. *see* MACLEOD, D. M.
BYRNE, F., ODURO-DOMINAH, A. & KIPLING, R. The effect of pregnancy on pulmonary nitrogen washout. A study of pre-oxygenation, 148

CALDER, I. *see* WHITLOCK, J. E.
CALHAEM, M. N. Multipurpose breathing systems: a reply, 88 (c)
CALHAEM, M. N. Another modification of the Nuffield 200 ventilator: a reply, 81 (c)
CALLANDER, C. C. Smoking and anaesthesia, 770 (c)
CALLANDER, C. C. & THOMAS, J. Modification of Macintosh laryngoscope for difficult intubation, 671 (c)

CAMERON, A. E. Opisthotonos again, 1124 (c)
CAMERON, E. W. J. *see* JENKINS, J.
CAMPBELL, D. M. *see* MACLENNAN, F. M.
CAMPBELL, I. T. *see* RAO, U.
CAMPBELL, P. C. *see* BROWN, T. C. K.
CAMPKIN, T. V. Cervical epidural analgesia during carotid artery surgery, 437 (c)
CARAPETIS, R. J. *see* RUNCIMAN, W. B.
CARDAN, E. & NANULESCU, M. Epidural lavage for extensive epidural suppuration, 1023 (c)
CARDAN, E., POP, R. & NEGRUTIU, S. Prolonged haemodynamic disturbance following attempted retrobulbar block, 668 (c)
CARL, P. *see* HØGSKILDE, S.
CARL, P. *see* WOLFF, J.
CARLI, F. *see* SHARPE, E.
CARTER, C. A. & WESTON, G. A. Fixed dilated pupils following cardiac surgery, 1231 (c)
CARTER, R. F. *see* ROY, R. C.
CARTWRIGHT, P. D. Obstetric epidural test doses, 556 (c)
CATLEY, D. M. *see* RAO, U.
CATLING, J. *see* CLAYTON, D.
CATTERMOLE, R. *see* FRANK, M.
CHAKRABARTI, M. K. *see* HARROP-GRIFFITHS, A. W.
CHAKRABARTI, M. K. *see* TWIGLEY, A.
CHANG, R. W. S. *see* JACOBS, S.
CHANNA, A. B., MOFTI, A. B., TAYLOR, G. W., MEKKI, M. O. & SHEIKH, M. H. Hypoglycaemic encephalopathy following surgery on phaeochromocytoma, 1298
CHAPMAN, I. *see* SCOTT, R. P. F.
CHARLTON, S. M. *see* PUSEY, J. M.
CHARTERS, P. Postmortem removal of tracheal tube, 1242 (c)
CHARTERS, P. & WILKINSON, K. Tactile orotracheal tube placement test. A bimanual tactile examination of the positioned orotracheal tube to confirm laryngeal placement, 801
CHARTERS, P., PERERA, S. & HORTON, W. A. Visibility of pharyngeal structures as a predictor of difficult intubation, 1115 (c)
CHATER, S. N. & SIMPSON, K. H. Response rates, 328 (c)
CHATER, S. N., GREIG, A. J. & SUGDEN, J. C. Epidural anaesthesia in the presence of a cerebral tumour, 433 (c)
CHATER, S. N. *see* SIMPSON, K. H.
CHAUSSAIN, M. *see* MURAT, I.
CHERALA, S., EDDIE, D., HALPERN, M. & SHEVDE, K. Priming with vecuronium in obstetrics, 1021 (c)
CHERALA, S. R. Prolonged neuromuscular blockade in a patient with a normal genotype, 214 (c)
CHERRY, D. A. *see* OWEN, H.
CHESTNUT, R. J. *see* KAY, B.
CHILD, C. S. B. Nebulised adrenaline, 322 (c)
CHONG, M. & DAVIS, T. P. Accidental intra-arterial injection of propofol, 781 (c)
CHOUDHRY, A. K. Nebulised adrenaline, 321 (c)
CHRISTENSEN, C. B. *see* KRANTZ, T.
CHUNARA, A. *see* HANNING, C. D.
CLAYTON, D. & CATLING, J. Safety of a new system for continuous airway pressure, 440 (c)
CLEMENTS, J. A. *see* OWEN, H.
COAD, N. R. Beta blockade and nitroprusside, 1022 (c)
CODY, M. W. & DORMON, F. M. Recurarisation after vecuronium in a patient with renal failure, 993
COE, A. J. Nitrous oxide and hearing loss, 1230 (c)
COHEN, A. T. & KELLY, D. R. Assessment of alfentanil by intravenous infusion as long-term sedation in intensive care, 545 (f)
COHEN, A. T. *see* WEBSTER, N. R.
COHEN, R. J. To chew or not to chew, 220 (c)
COLEMAN, P. & PHILLIPS, B. Propofol in failed tracheal intubation, 1233 (c)
COLLETT, B. J. *see* GUNNING, K. E. J.
COLLETT, B. J. *see* LINDSAY, S. L.
COLLIER, P. S. *see* WILSON, C. M.
COLNE, R. Y. *see* POLSON, R. J.
COLVILLE, L. J. *see* MACMILLAN, R. R.
CONACHER, I. D., PAES, M. L. & MORRITT, G. N. Carbon dioxide laser bronchoscopy. A review of problems and complications, 511
CONACHER, I. D. *see* MORGAN, B. A.
CONDON, H. A. Brünings' bronchoscopic mask, 996
CONDON, H. A. Sir Ivan Magill. A supplementary bibliography, 1096

COOMBS, T. J. Graseby PCAS pumps—a potential hazard: a reply, 560 (c)
COOPER, C. M. S. A test for breathing systems, 1019 (c)
COOPER, C. M. S. Capnography, 1238 (c)
COOPER, C. M. S. Pleural aspiration with a central venous catheter, 217 (c)
COOPER, C. M. S. & MURRAY-WILSON, A. Retrograde intubation. Management of a 4.8-kg, 5-month infant, 1197
COPPEL, D. L., *see* MCCARTHY, G.
CORKILL, C. M. *see* MCNAMEE, R.
COSGROVE, J. *see* MCCARTHY, G.
COTTINGHAM, R. L. Beating the blocked balloon, 673 (c)
COVENTRY, D. M., MCMENEMIN, I. & LAWRIE, S. Bradycardia during intra-abdominal surgery. Modification by preoperative anticholinergic agents, 835
COZANITIS, D. A., POUTTU, J. & ROSENBERG, P. H. Bradycardia associated with the use of vecuronium. A comparative study with pancuronium with and without glycopyrronium, 192 (f)
CRAWFORD, J. S. A prospective study of 200 consecutive twin deliveries, 33
CRAWFORD, J. S. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1229 (c)
CRAWFORD, J. S. Epidural block for Caesarean section: a reply, 327 (c), 435 (c)
CRAWFORD, J. S. Epidural anaesthesia for elective Caesarean section: a reply, 555 (c)
CRAWFORD, M. E. *see* WOLFF, J.
CRIPPS, T. P. & EDMONDSON, R. S. Isoflurane for anaesthesia in the dental chair. A comparison of the incidence of cardiac dysrhythmias during anaesthesia with halothane and isoflurane, 189 (f)
CROSS, G. D. Simple device for the assessment of local anaesthetic blocks in children, 84 (c)
CROSS, G. D. & BARRETT, R. F. Comparison of two regional techniques for postoperative analgesia in children following herniotomy and orchidopexy, 845
CROZIER, W. C. Upper airway obstruction in neurofibromatosis, 1209
CRUL, J. F. *see* DE GROOD, P. M. R. M.
CUNDY, J. M. Recovery times, 89 (c)
CUNDY, J. M. *see* LUKE, J. J.
CYRIAC-MATHEW, A. *see* KARTHA, R. K.

DALE, B. A. B. *see* SIMPSON, D. L.
DALSGAARD, P. F. *see* JACOBSEN, J.
DAVENPORT, J. *see* SYNNOTT, A.
DAVIDSON, J. T. *see* ELDOR, J.
DAVIE, R. A. *see* RAILTON, R.
DAVIES, C. A. & GRANT, I. S. Total collapse of lung and CPAP, 780 (c)
DAVIES, G. *see* BLOM, H. J.
DAVIES, J. M. *see* STRUNIN, L.
DAVIES, J. R. Broken control on a Selectatec vaporizer, 215 (c)
DAVIS, I. Intra-operative myocardial ischaemia: a reply, 1127 (c)
DAVIS, I. Intrathecal morphine in aortic aneurysm surgery, 491
DAVIS, T. P. *see* CHONG, M.
DAYKIN, A. P. *see* BOWEN, D. J.
DEAR, G. DE L., HAMMERTON, M., HATCH, D. J. & TAYLOR, D. Anaesthesia and intra-ocular pressure in young children. A study of three different techniques of anaesthesia, 259
DE GROOD, P. M. R. M., HARBERS, J. B. M., VAN EGMOND, J. & CRUL, J. F. Anaesthesia for laparoscopy. A comparison of five techniques including propofol, etomidate, thiopentone and isoflurane, 815
DE GROOD, P. M. R. M., MITSUKURI, S., VAN EGMOND, J., RUTTEN, J. M. J. & CRUL, J. F. Comparison of etomidate and propofol for anaesthesia in microlaryngeal surgery, 366
DE LANGE, J. J. *see* TREFFERS, R.
DESCORPS-DECLERE, A. *see* BRASSEUR, L.
DIAGO, C. *see* SOLARES, G.
DIMOPOULOS, C. *see* ECONOMACOS, G.
DINGWALL, A. E. Oculogyric crisis after day case anaesthesia, 565 (c)
DIVEKAR, V. M. Betel nut chewing, 900 (c)
DIXON, J. Primary amyloidosis and skin damage, 217 (c)
DIXON, J. *see* SANGALA, W.
DODD, K. W. *see* LEE, A.
DOLGUNSKI, E. *see* JEDEIKIN, R.
DOLLERY, W. C. *see* MACLEOD, D. M.
DONADONI, R. & ROLLY, G. Epidural sufentanil versus intramuscular buprenorphine for postoperative analgesia. A double-blind comparative trial, 1171
DORMÒN, F. *see* PURCELL-JONES, G.
DORMON, F. M. *see* CODY, M. W.
DORRINGTON, K. L. & LEHANE, J. R. Minimum fresh gas flow requirements of anaesthetic breathing systems during spontaneous ventilation: a graphical approach, 732

DOUGALL, J. R. *see* MILLER, C. D.
DOW, A. A. C. & WILKINS, R. G. Marcain shakes, 328 (c)
DOWNING, J. W. *see* MITCHELL, M. D.
DRAKE, H. F., TREASURE, T. and SMITH, B. Continuous display of plasma potassium during cardiac surgery, 23
DRIESSEN, J. J. *see* VAN DIEJEN, D.
DRUMMOND, G. B. Intratracheal pressure during controlled ventilation in infants, 1332 (c)
DUMAIS, R. *see* MARTIN, R.
DUMONT, S. M. & MOUSDALE, S. A basic problem at cardiac arrests, 1018 (c)
DUNCAN, B. *see* SALE, J. P.
DUNDAS, C. R., LEVACK, I. D. & BROCKWAY, M. S. Monitoring neuromuscular blockade. The table knife transducer, 1092
DUNDEE, J. W., LYNAS, A. G. A. & GHALY, R. G. Alternative medicine, 76 (c)
DUNDEE, J. W. *see* FURNESS, G.
DUNDEE, J. W. *see* GHALY, R. G.
DUNDEE, J. W. *see* MILLIGAN, K. R.
DUNDEE, J. W. *see* O'TOOLE, D. P.
DUNDEE, J. W. *see* WILSON, C. M.
DURKIN, M. A. *see* FENECK, R. D.
DUTHIE, D. J. R., MONTGOMERY, J. N., SPENCE, A. A. & NIMMO, W. S. Concurrent drug therapy in patients undergoing surgery, 305 (f)
DUTTON, D. *see* MORRISON, C. E.
DYE, D. J. *see* EMMANUEL, E. R.

EASON, J. R., SWAINE, C. N. & JONES, P. I. E. Unstable cervical fracture, 1334 (c)
EASON, J. R., SWAINE, C. N., JONES, P. I. E., GRONOW, M. J. & BEAUMONT, A. Unstable cervical fracture. Anaesthetic management for an urgent Caesarean section, 745
EASTLEY, R. J. *see* HANNING, C. D.
ECONOMACOS, G., LOUKAS, S., MANTZOURATOS, D. & DIMOPOULOS, C. Extracorporeal shock wave lithotripsy, 779 (c)
EDDIE, D. *see* CHERALA, S.
EDDLESTONE, J. M. Pyrexia associated with a retroperitoneal tumour, 213 (c)
EDMONDSON, L. & ERWIN, D. C. Spinal anaesthesia in pregnant patients, 666 (c)
EDMONDSON, L. *see* MASON, D. G.
EDMONDSON, R. S. *see* CRIPPS, T. P.
EDRIDGE, A. W. Sir Ivan Whiteside Magill, KCVO, DSC(Hon), MB, BCh, BAO, FRCS (Hon), FFARCS (Hon), FFARCSI (Hon), DA, 23 July 1888–25 November 1986: editorial, 231
EDWARDS, J. D. *see* WILKINS, R. G.
ELDOR, J., HOFFMAN, B. & DAVIDSON, J. T. Prolonged bradycardia and hypotension after neostigmine administration in a patient receiving atenolol, 1294
ELLING, A. E. *see* MEIKLEJOHN, B. H.
ELLIOTT, P. *see* MIRAKHUR, R. K.
ELPHINSTONE, M. G. & GRANT, I. S. Persistent pneumothorax treated with continuous positive airway pressure, 987
ELTRINGHAM, R. J. & FAIRBAIRN, M. L. Hypotensive anaesthesia for middle ear surgery: a reply, 669 (c)
EMMANUEL, E. R. & DYE, D. J. Unwanted equipment, 220 (c)
ERWIN, D. C. *see* EDMONDSON, L.
EVANS, C. S. *see* BICKFORD-SMITH, P.
EVANS, K. T. *see* YUKIOKA, H.
EWART, M. C. & RUBIN, A. P. Subarachnoid block with hyperbaric lignocaine. A comparison with hyperbaric bupivacaine, 1183

FAHY, L. T. Delayed convulsions after day case anaesthesia with enflurane, 1327 (c)
FAIRBAIRN, M. L. *see* ELTRINGHAM, R. J.
FAITHFULL, N. S. Fluorocarbons. Current status and future applications, 234
FARMAN, J. V. *see* LINDOP, M. J.
FARMAN, J. V. *see* POLSON, R. J.
FELDMAN, S. A. & LIBAN, J. B. Vecuronium—a variable dose technique, 199 (f)
FELL, D. *see* PINNOCK, C. A.
FENECK, R. O. & DURKIN, M. A. A comparison between the effects of fentanyl, droperidol with fentanyl, and halothane anaesthesia on intra-ocular pressure in adults, 266
FENECK, R. O. *see* NORMANDALE, J.
FENECK, R. O. *see* SHERRY, K. M.
FINFER, S. R. & WISHAW, K. J. Oximetry during transport, 900 (c)
FINLAY-MILLS, B. M. *see* JACK, T. M.
FITZPATRICK, K. T. J. *see* GHALY, R. G.
FLAATTEN, H., RODT, S., ROSLAND, J. & VAMNES, J. Postoperative headache in young patients after spinal anaesthesia, 202 (f)

FLETCHER, R. All that wheezes is not asthma—yet again, 441 (c)
FLETCHER, R. Arterial to end tidal CO_2 tension differences, 210 (c)
FLETCHER, R. 4th International Malignant Hyperpyrexia Workshop. Report of a meeting, 206
FLYNN, P. J. *see* BONE, M. E.
FOG, J. *see* WANG, L. P.
FORREST, T. & RAMAGE, D. T. O. Cardiac dysrhythmia after subtrigonal phenol, 777 (c)
FORTUNA, A. Narcoanalgesia, 329 (c)
FORTUNE, D. W. *see* PAULL, J. D.
FRANCIS, G. A. Epidural anaesthesia in the presence of a cerebral tumour, 434 (c)
FRANK, M., MCATEER, E. J., CATTERMOLE, R., LOUGHNAN, B., STAFFORD, L. B. & HITCHCOCK, A. M. Nalbuphine with pethidine for pain relief in labour when administered by patient-controlled analgesia (PCA), 697
FRASER, G. *see* PRINCE, G. D.
FRAZER, S. *see* RUSSELL, G. N.
FROST, P. M. Patients with problems, 328 (c)
FURNESS, G., DUNDEE, J. W. & MILLIGAN, K. R. Low dose sufentanil pretreatment. Effect on the induction of anaesthesia with thiopentone, methohexitone or midazolam, 1264

GABRIEL, P. *see* BRASSEUR, L.
GALLAGHER, J., STRANGEWAYS, J. E. M. & ALLT-GRAHAM, J. Contamination control in long-term ventilation. A clinical study using a heat- and moisture-exchanging filter, 476
GALLAGHER, J. *see* ALLT-GRAHAM, J.
GALLER, D. *see* BONE, M. E.
GALLOWAY, D. W. Rapid inhalation induction, 772 (c)
GAUKROGER, P. B. *see* OWEN, H.
GAUNTLETT, I. S. Analgesia for neonates, 1328 (c)
GAYLARD, D. G., WILSON, I. H. & BALMER, H. G. R. An epidural infusion technique for labour, 1098 (f)
GEORGE, M. A. *see* PURI, G. D.
GERAGHTY, I. *see* HILL, H.
GHALY, R. G., FITZPATRICK, K. T. J. & DUNDEE, J. W. Antiemetic studies with traditional Chinese acupuncture. A comparison of manual needling with electrical stimulation and commonly used antiemetics, 1108 (f)
GHALY, R. G. *see* DUNDEE, J. W.
GIBBONS, J. R. *see* MCCARTHY, G.
GILBERT, J., HOLT, J. E., JOHNSTON, J., SABO, B. A. & WEAVER, J. S. Intravenous sedation for cataract surgery, 1063
GILLBE, C. E. *see* SMITH, D. C.
GILLIES, G. W. A., KENNY, G. N. C., BULLINGHAM, R. E. S. & MCARDLE, C. S. The morphine sparing effect of ketorolac tromethamine. A study of a new, parenteral non-steroidal anti-inflammatory agent after abdominal surgery, 727
GILLIES, G. W. A. *see* HODSMAN, N. B. A.
GILMOUR, H. *see* MORRISON, C. E.
GILSTON, A. Should ventilator alarms be compulsory?, 667 (c)
GOAT, V. A. *see* WAIT, C. M.
GODDARD, J. M. & BOOKER, P. D. The use of bronchial stents in the management of bronchomalacia, 534
GOLDBERG, P. L. Disconnexion hazard, 219 (c)
GOLDHILL, D. R. & MARTYN, J. A. J. Beta blockade, suxamethonium and potassium, 670 (c)
GOLDHILL, D. R. *see* MARTYN, J. A. J.
GOLDMANN, L., SHAH, M. V. & HEBDEN, M. W. Memory of cardiac anaesthesia. Psychological sequelae in cardiac patients of intra-operative suggestion and operating room conversation, 596
GOLDSTONE, J. C. & PENNANT, J. H. Spinal anaesthesia following facet joint injection. A report of two cases, 754
GOROSZENIUK, T. & WRIGHT, J. T. Epidural anaesthesia in the presence of a cerebral tumour: a reply, 434 (c)
GOSS, I. J. *see* HINTON, W.
GOURLAY, G. K. *see* OWEN, H.
GRANT, I. S. & MACKENZIE, N. Relative potency of propofol and thiopentone, 317 (c)
GRANT, I. S. *see* DAVIES, C. A.
GRANT, I. S. *see* ELPHINSTONE, M. G.
GRANT, I. S. *see* MACKENZIE, N.
GRAZIOTTI, P. J. Atriobronchial fistula: an unusual complication of intravenous feeding in the presence of a mediastinal abscess, 669 (c)
GREBENIK, C. R., ORLIKOWSKI, C. & BARBER, J. D. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1227 (c)
GREEN, R. A. A matter of vigilance: a reply, 313 (c), 435 (c)
GREENBAUM, R. Down the tube: editorial, 927
GREGORY, M. *see* BROWN, T. C. K.
GREIG, A. J. *see* CHATER, S. N.
GRIFFIN, R. M. Intra-operative myocardial ischaemia, 1127 (c)
GRIFFIN, R. M. & KAPLAN, J. A. Myocardial ischaemia during non-cardiac surgery, 155

GRIFFITHS, R. B., HORTON, W. A., JONES, I. G. & BLAKE, D. Speed of injection and spread of bupivacaine in the epidural space, 160
GRONOW, M. J. *see* EASON, J. R.
GROUNDS, R. M., TAYLOR, M. B. & MORGAN, M. Relative potency of propofol and thiopentone: a reply, 318 (c)
GROVER, V. K., SHARMA, S., MAHAJAN, R. P. & SINGH, H. Intranasal nitroglycerine attenuates pressor response to tracheal intubation in beta-blocker treated hypertensive patients, 884 (f)
GROVES, N. D., REES, J. L. & ROSEN, M. Effects of benzodiazepines on laryngeal reflexes. Comparison of lormetazepam and Diazemuls, 808
GRUNDY, E. M. *see* BRAY, B. M.
GUNNING, K. E. J. & COLLETT, B. J. Spontaneous retrobulbar haemorrhage following anaesthesia, 875
GUSBERG, R. J. *see* SMITH, G. B.
GWINNUTT, C. L. & LORD, W. D. Nebulised adrenaline, 320 (c)

HAIN, W. R. *see* STANDEN, P. J.
HALL, I. *see* O'DEA, J.
HALL, P. J. *see* MILLAR, J. M.
HALL, R. M. *see* ALLEN, S. C.
HALPERN, M. *see* CHERALA, S.
HALSEY, M. J. *see* STRUBE, P. J.
HALWORTH, D. *see* SINCLAIR, J. F.
HAMMERTON, M. *see* DEAR, G. DE L.
HAMZA, J. *see* MURAT, I.
HANKS, G. W., HOSKIN, P. J. & WALKER, V. A. Diamorphine stability and pharmacodynamics, 664 (c)
HANKS, G. W., TWYCROSS, R. G. & BLISS, J. M. Controlled release morphine tablets: a double-blind trial in patients with advanced cancer, 840
HANKS, G. W. *see* JACK, T. M.
HANNING, C. D., KRUCHEK, D. & CHUNARA, A. Preferential oxygen leak—an unusual case, 1329 (c)
HANNING, C. D., LEW, J. & EASTLEY, R. J. Oxygenation during electroconvulsive therapy, 1234 (c)
HANNING, C. D., LEW, J. & EASTLEY, R. J. Oxygenation during electroconvulsive therapy: a reply, 432 (c)
HANNING, C. D., OGDEN, B. & PARRY, P. Graseby PCAS pumps—a potential hazard, 559 (c)
HANSON, G. C. *see* LINDSAY, S. L.
HARBERS, J. B. M. *see* DE GROOD, P. M. R. M.
HARDING, C. J. & MCVEY, F. K. Interview method effects incidence of postoperative sore throat, 1104 (f)
HARPER, S. J. *see* UNDERHILL, S.
HARRINGTON, J. M. The health of anaesthetists: editorial, 131
HARRIS, M. N. E. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1229 (c)
HARRIS, R. *see* REID, M. F.
HARROP-GRIFFITHS, A. W., CHAKRABARTI, M. K. & WHITWAM, J. G. High frequency ventilation and afferent vagal activity, 1162
HASKEL, Y. *see* VATASHSKY, E.
HATCH, D. J. *see* DEAR, G. DE L.
HATCH, D. J. *see* LINDAHL, S. G. E.
HAYWARD, M. W. J. *see* YUKIOKA, H.
HEALY, T. E. J. *see* KAY, B.
HEBDEN, M. W. *see* GOLDMANN, L.
HEDLEY, R. *see* TRAN, Y.
HELMERS, J. H. J. H. *see* ZUURMOND, W. W. A.
HENDERSON, A. M., VALLIS, C. J. & SUMNER, E. Anaesthesia in the prune-belly syndrome. A review of 36 cases, 54
HENDERSON, A. M. *see* MARYNIAK, J. K.
HERREGODS, L., ROLLY, G., VERSICHELEN, L. & ROSSEEL, M. T. Propofol combined with nitrous oxide–oxygen for induction and maintenance of anaesthesia, 360
HIGGINS, M. *see* THORP, J. M.
HILL, H., GERAGHTY, I., HUGHES, A., SEVER, P. S. & SCHACHTER, M. Ergometrine and bronchospasm, 1115 (c)
HILLMAN, K. M. Peri-operative fluids: a reply, 571 (c)
HILLS, B. A. Bursting the alveolar bubble: editorial, 467
HINDOCHA, N. *see* MEIKLEJOHN, B. H.
HINDS, C. J. A way forward for intensive care, 551 (c)
HINTON, W. & GOSS, I. J. Croup, nubulised adrenaline and preservatives, 436 (c)
HITCHCOCK, A. M. *see* FRANK, M.
HODSMAN, N. B. A., BURNS, J., BLYTH, A., KENNY, G. N. C., MCARDLE, C. S. & ROTMAN, H. The morphine sparing effects of diclofenac sodium following abdominal surgery, 1005 (f)
HODSMAN, N. B. A., KENNY, G. N. C., GILLIES, G. W. A. & MCARDLE, C. S. Feedback during patient-controlled analgesia using a speech synthesiser, 767 (f)
HOFFMAN, B. *see* ELDOR, J.
HOFFMAN, S. *see* JEDIEKIN, R.

HØGSKILDE, S., NIELSEN, J. W., CARL, P. & SØRENSEN, M. B. Pregnanolone emulsion. A new steroid preparation for intravenous anaesthesia: an experimental study in mice, 586

HØGSKILDE, S., WAGNER, J., CARL, P. & SØRENSEN, M. B. Anaesthetic properties of pregnanolone emulsion. A comparison with alphaxolone/alphadolone, propofol, thiopentone and midazolam in a rat model, 1045

HOLE, P. *see* MEHTA, Y.

HOLK, I. K. *see* JENSEN, F. M.

HOLLIS, N., WHITE, J. B. & PROCTER, A. J. M. Spinal anaesthesia for Caesarean section, 323 (c)

HOLT, J. E. *see* GILBERT, J.

HOMI, J. *see* MOSELEY, H.

HOMMELGAARD, P. *see* LARSEN, U. T.

HORSEY, P. J. Nomenclature of circle absorption breathing systems, 1018 (c)

HORSEY, P. J. *see* SADDLER, J. M.

HORTON, W. A. *see* CHARTERS, P.

HORTON, W. A. *see* GRIFFITHS, R. B.

HOSKER, K. J. *see* STANDEN, P. J.

HOSKIN, P. J. *see* HANKS, G. W.

HOUGHTON, I.T. *see* YOGANATHAN, S.

HOWARD, E. C. *see* KIRBY, I. J.

HOWARD, P. J. *see* WILSON, C. M.

HOWARD, R. C. *see* MILLIGAN, K. R.

HOWE, J. P. *see* O'TOOLE, D. P.

HOWELL, P. J. & BAMBER, P. A. Severe acute anaemia in a Jehovah's Witness. Survival without blood transfusion, 44

HOWELLS, T. H. The cricoid yoke: a rely, 781 (c)

HOWIE, H. *see* MORRISON, C. E.

HUGHES, A. *see* HILL, H.

HUGHES-DAVIES, D. I. A nerve palsy occurring during the recovery period, 326 (c)

HULANDS, G. H. *see* STRUBE, P. J.

HUMPHREY, D. Multipurpose breathing systems, 88 (c)

HUNSLEY, C. Evaluation of oxygen analysers, 1127 (c)

HUNTER, D. N., THORNILY, A. & WHITBURN, R. Arousal from propofol, 1128 (c)

HUNTER, J. M. Pancuronium and renal failure, 1236 (c)

HUNTER, J. M. *see* SMITH, C. L.

HUNTER, R. M. *see* JENKINS, J.

HUNTON, J. & OSWAL, V. H. Anaesthetic management for carbon dioxide laser surgery in tracheobronchial lesions, 1222 (f)

HUTCHINSON, R. Early retirement and morbidity, 1024 (c)

HUTCHISON, G. L. The severance of epidural catheters, 182

HUTCHISON, G. L. The severance of epidural catheters: a reply, 315 (c)

HUTTER, C. D. D. Bradycardia and hypotension in spinal anaesthesia, 89 (c)

ILSLEY, A. H. *see* RUNCIMAN, W. B.

JACK, T. M. An unusual cause of complete expiratory obstruction, 564 (c)

JACK, T. M., WALKER, V. A., MORLEY, S. J., HANKS, G. W. & FINLAY-MILLS, B. M. Depression, anxiety and chronic pain, 1235 (c)

JACKSON, I. J. B. *see* MCQUILLAN, P. J.

JACOBS, S., CHANG, R. W. S. & LEE, B. One year's experience with the APACHE II severity of disease classification system in a general intensive care unit, 738

JACOBSEN, J., BACH, A. B. & DALSGAARD, P. F. Blood tests before elective surgery, 78 (c)

JAGO, R. H. *see* ALLEN, S. C.

JAMES, M. F. M. A new ventilator for closed breathing systems, 1335 (c)

JAMES, R. H. A matter of viligance, 313 (c)

JAMES, R. H. *see* TANSKI, J.

JEDEIKIN, R., DOLGUNSKI, E., KAPLAN, R. & HOFFMAN, S. Prolongation of neuromuscular blocking effect of vecuronium by antibiotics, 858

JENKINS, J., CAMERON, E. W. J., MILNE, A. C. & HUNTER, R. M. One lung anaesthesia. Cardiovascular and respiratory function compared during conventional ventilation and high frequency jet ventilation, 938

JENSEN, F. M., JENSEN, N.-H., HOLK, I. K. & RAVNBORG, M. Prolonged and biphasic respiratory depression following epidural buprenorphine, 470

JENSEN, N.-H. *see* JENSEN, F. M.

JOHNSTON, I. G. *see* YOGANATHAN, S.

JOHNSTON, J. *see* GILBERT, J.

JOHNSTON, K. R. Postmortem removal of tracheal tube, 1242 (c)

JONES, C. J. *see* MIRAKHUR, R. K.

JONES, H. M. *see* BRAY, B. M.

JONES, H. M. *see* SHERRY, K. M.
JONES, I. G. *see* GRIFFITHS, R. B.
JONES, M. J. *see* BLOOR, G. K.
JONES, P. I. E. *see* EASON, J. R.
JONES, R. M. & ROSEN, M. Smoking and anaesthesia: a reply, 771 (c)
JONES, R. M., ROSEN, M. & SEYMOUR, L. Smoking and anaesthesia: editorial, 1
JONES, R. S. Limitations of the Grass FT03 transducer: a reply, 85 (c)
JONES, R. S. *see* SMITH, C. L.
JONES, S. *see* WARRAN, P.
JORDAN, R. H. *see* SMITH, G. B.
JUSTINS, D. M. *see* PURCELL-JONES, G.

KAANDERS, J. H. A. M. *see* VAN DIEJEN, D.
KAINUMA, M. & SHIMADA, Y. Cervical epidural analgesia during carotid surgery: a reply, 438 (c)
KAINUMA, M. & SHIMADA, Y. If nothing goes wrong—is everything alright?: a reply, 558 (c)
KALLA, G. N. A protocol for safety, 667 (c)
KAPLAN, J. A. *see* GRIFFIN, R. M.
KAPLAN, R. *see* JEDEIKIN, R.
KARSDORP, V. *see* BLOM, H. J.
KARTHA, R. K. & CYRIAC-MATHEW, A. Transnasal anaesthesia of the pharynx, larynx and trachea, 320 (c)
KAY, B. Relative potency of propofol and thiopentone, 1025 (c)
KAY, B., CHESTNUT, R. J., SUM PING, J. S. T. & HEALY, T. E. J. Economy in the use of muscle relaxants. Vecuronium after pancuronium, 277
KAY, B., NOLAN, D., MAYALL, R. & HEALY, T. E. J. The effect of sufentanil on the cardiovascular responses to tracheal intubation, 382
KEELING, P. Nitrous oxide in early pregnancy, 211 (c)
KEELING, P. A. *see* SHERRY, K. M.
KEEN, R. I. Spontaneous ventilation in old people, 568 (c)
KEEN, R. I. & MCNAMEE, R. Early retirement and morbidity, 1024 (c)
KEEN, R. I. *see* MCNAMEE, R.
KELLY, D. R. *see* COHEN, A. T.
KENNY, G. N. C. *see* GILLIES, G. W. A.
KENNY, G. N. C. *see* HODSMAN, N. B. A.
KENNY, G. N. C. *see* MCMENEMIN, I. M.
KENT, A. P. Humidification by filters, 1119 (c)
KERRIDGE, R. *see* LINDSAY, S. L.
KERTÉSZ, A. Plasma hormone measurements following midazolam administration, 562 (c)
KESTIN, I. G. Flow through intravenous cannulae, 67
KESTIN, I. G. Pressure–flow relationships in intravenous infusion systems: a reply, 776 (c)
KIM, B. *see* SMITH, G. B.
KINNEAR, W. *see* MANARA, A. R.
KINSELLA, J. Epidural anaesthesia in the presence of a cerebral tumour, 433 (c)
KINSELLA, S. M. Needlestick injury from indwelling steel needle, 900 (c)
KIPLING, R. M. & BETHUNE, D. W. Passive or active scavenging systems?, 777 (c)
KIPLING, R. *see* BYRNE, F.
KIRBY, I. J. & HOWARD, E. C. Propofol in a morbidly obese patient, 1125 (c)
KIRKPATRICK, T. Contamination of ampoules, 779 (c)
KIRKWOOD, I. Spinal anaesthesia for Caesarean section, 899 (c)
KJELDSEN, L. Transvenous misplacement and loop formation of spring guide wire, 216 (c)
KNIGHT, B. H. & ADDICOTT, L. S. Postmortem removal of tracheal tube: a legal opinion, 554 (c)
KOCAN, M. The Triservice anaesthetic apparatus. Trial of isoflurane and enflurane as alternatives to halothane, 1101 (f)
KONARZEWSKI, W. H., RICHARDS, G., THOMSON, S. & NASH, D. G. Explosive anaesthetic agents. A regional survey on the use of ether and cyclopropane, 186 (f)
KRANTZ, T. & CHRISTENSEN, C. B. Respiratory depression after intrathecal opioids. Report of a patient receiving long-term epidural opioid therapy, 168
KRISHNAN, A. *see* SHANKAR, K. B.
KRUCHEK, D. *see* HANNING, C. D.
KUBOTA, H. *see* KUBOTA, Y.
KUBOTA, Y., TOYODA, Y., KUBOTA, H. & UEDA, Y. Shaping tracheal tubes, 896 (c)
KUMAR, A. Y. *see* MOSELEY, H.
KUMAR, C. M. Epidural buprenorphine for postoperative analgesia, 79 (c)
KUMAR, Y. *see* SHANKAR, K. B.
KURTZ, J. B. *see* SINCLAIR, M. E.
KUWELKER, M. D. & LAWLER, P. G. Nasotracheal intubation: a problem with another approach, 442 (c)

KWAN, J. Y. & SEE, T. Y. Another modification of the Nuffield 200 ventilator, 80 (c)

LAGHARI, N. A. *see* VAN DEN BERG, A. A.
LAISHLEY, R. S. Manufactured drug dilutions for paediatric anaesthesia, 213 (c)
LAISHLEY, R. S., REYNOLDS, F. & MORGAN, B. M. Epidural anaesthesia for elective Caesarean section, 554 (c)
LAMBERTY, J. M. Cyclopropane, 212 (c)
LAMBOURNE, A. *see* VAN DEN BERG, A. A.
LARSEN, U. T. & HOMMELGAARD, P. Pneumatic torniquet paralysis following intravenous regional analgesia, 526
LARSON, M. D. Action of narcotics on the pupil, 566 (c)
LATIMER, R. *see* BODENHAM, A.
LAURENCE, A. S. Myalgia and biochemical changes following intermittent suxamethonium administration. Effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on serum myoglobin, creatine kinase and myalgia, 503
LAVERY, G. G. *see* MIRAKHUR, R. K.
LAVIES, N. G. Speed of epidural injection, 783 (c)
LAWLER, P. G. *see* KUWELKER, M. D.
LAWRIE, S. *see* COVENTRY, D. M.
LEACH, K. G. *see* YUKIOKA, H.
LEDINGHAM, I. MCA. *see* NEWMAN, L. H.
LEE, A. & DODD, K. W. Accidental subdural catheterisation: a reply, 557 (c)
LEE, B. *see* JACOBS, S.
LEE, K. G. *see* SONI, N.
LEHANE, J. R. *see* DORRINGTON, K. L.
LENOIR, R. J. Severe acute asthma and the menstrual cycle, 1287
LETT, Z. Children and explosive anaesthetics, 443 (c)
LEUNG, K. B. P. *see* WITHINGTON, D. E.
LEVACK, I. D. *see* DUNDAS, C. R.
LEW, J. *see* HANNING, C. D.
LIBAN, J. B. *see* FELDMAN, S. A.
LIBERMAN, H. *see* VONWILLER, J. B.
LIM, M. *see* MARYNIAK, J. K.
LINDAHL, S. G. E., YATES, A. P. & HATCH, D. J. Respiratory depression in children at different end tidal halothane concentrations, 1267
LINDOP, M. J., FARMAN, J. V., SMITH, M. F. & THOMAS, D. G. Haemonetic cell saver, 85 (c)
LINDOP, M. J. *see* POLSON, R.J.
LINDSAY, S. L. & HANSON, G. C. Cardiac arrest in near-term pregnancy, 1074
LINDSAY, S. L. & MASON, D. F. Hypophosphataemia, 439 (c)
LINDSAY, S. L., KERRIDGE, R. & COLLETT, B.-J. Abscess following cannulation of the radial artery, 654
LLOYD, E. L. Hallucinations after anaesthesia, 1015 (c)
LLOYD, E. L. Treatment of accidental hypothermia with the Clinitron bed, 1121 (c)
LOCKHART, A. *see* MOSTAFA, S. M.
LOCKYER, J. A. *see* SIMPSON, P. J.
LORD, W. D. *see* GWINNUTT, C. L.
LOUGHNAN, B. *see* FRANK, M.
LOUGHNAN, B. L., SEBEL, P. S., THOMAS, D., RUTHERFORD, C. F. & ROGERS, H. Evoked potentials following diazepam or fentanyl, 195 (f)
LOUKAS, S. *see* ECONOMACOS, G.
LOWE, G. D. Efficiency of heat and moisture exchangers: a reply, 1118 (c)
LUKE, J. J. & CUNDY, J. M. AIDS and anaesthesia, 1242 (c)
LUNN, J. N. *see* MATHIAS, J. A.
LYNAS, A. G. A. *see* DUNDEE, J. W.

MCARDLE, C. S. *see* GILLIES, G. W. A.
MCARDLE, C. S. *see* HODSMAN, N. B. A.
MCATEER, E. J. *see* FRANK, M.
MCCARTHY, G., COPPEL, D. L., GIBBONS, J. R. & COSGROVE, J. High frequency jet ventilation for bilateral bullectomy, 411
MCCOLLUM, J. S. C. *see* O'TOOLE, D. P.
MCCONACHIE, I. Value of pre-operative carotid sinus massage, 636
MACDONALD, A. F. *see* MACLENNAN, F. M.
MCDONALD, J. C. *see* NEWMAN, L. H.
MACDONALD, R. *see* PHILLIPS, D. C.
MCDOWELL, J. M. A matter of vigilance, 313 (c)
MACGILLIVRAY, R. G., ROCKE, D. A. & MAHOMEDY, A. E. Correct placement of bronchial tubes, 570 (c)
MCGRADY, E. M. Management of labour and delivery in a patient with Guillain–Barré syndrome, 899 (c)

MCGREGOR, P. J. Guide-wire assisted arterial cannulation—a complication: a reply, 563 (c)
MCGUINN, W. J. *see* MALINOW, A. M.
MCHUGH, P. *see* MASON, D. G.
MACKECHNIE, S. Smoking and anaesthesia, 771 (c)
MACKENZIE, I. *see* THORP, J. M.
MACKENZIE, J. W. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1229 (c)
MCKENZIE, N. & GRANT, I. S. Propofol for intravenous sedation, 3
MCKENZIE, N. *see* GRANT, I. S.
MCKEOWN, D. W. *see* PAUL, D. L.
MACKIE, A. Reservoir volume in a drawover system, 1337 (c)
MACKIE, A. M. Drawover anaesthetic systems. Factors determining the inspired oxygen concentration, 299
MACKIE, D. S. Ventolin nebules, 1332 (c)
MCKINNEY, M. S. Hanging drop and extradural pressures, 1123 (c)
MACLENNAN, F. M., MACDONALD, A. F. & CAMPBELL, D. M. Lung water during the puerperium, 141
MACLEOD, D. M., TEY, H. K., BYERS, G. F., DOLLERY, W. C. & TUNSTALL, M. E. The loading dose for continuous infusion epidural analgesia. A technique to reduce the incidence of hypotension, 377
MCMENEMIN, I. M. & KENNY, G. N. C. Guide-wire assisted arterial cannulation—a complication, 562 (c)
MCMENEMIN, I. *see* COVENTRY, D. M.
MACMILLAN, R. R. & COLVILLE, L. J. Repeated use of halothane, 1017 (c)
MCNAMEE, R., KEEN, R. I. & CORKILL, C. M. Morbidity and early retirement among anaesthetists and other specialists, 133
MCNAMEE, R. *see* KEEN, R. I.
MCNICOL, L. R. Quality of axillary brachial plexus block, 774 (c)
MCNICOL, L. R. *see* SHERLOCK, D. A.
MCQUILLAN, P. J. & JACKSON, I. J. B. Potential leaks from anaesthetic machines. Potential leaks through open Rotameter valves and empty cylinder yokes, 1308
MACRAE, D. J. Diamorphine in aqueous solution, 82 (c)
MACRAE, W. R. *see* SIMPSON, D. L.
MCVEY, F. K. *see* HARDING, C. J.
MCWILLIAMS, D. M. *see* ALLEN, S. C.
MADEJ, T. H. & STRUNIN, L. Comparison of epidural fentanyl with sufentanil. Analgesia and side effects after a single bolus dose during elective Caesarean section, 1156
MADEJ, T. H., WATSON, N. C. & MARTIN B. C. Large dose epidural sufentanil. Management of postoperative pain with few side effects, 1204
HAHAJAN, R. P. *see* GROVER, V. K.
MAHOMEDY, A. E. *see* MACGILLIVRAY, R. G.
MAJOR, E. A. A way forward for intensive care, 553 (c)
MALCOLM, G. A. *see* SINCLAIR, J. F.
MALINOW, A. M., RICKFORD, W. J. K., MOKRISKI, B. L. K., SALLER, D. N. & MCGUINN, W. J. Lupus anticoagulant. Implications for obstetric anaesthetists, 1291
MANARA, A. R. Brachial plexus block. Unilateral thoraco-abdominal blockade following the supraclavicular approach, 757
MANARA, A. R., KINNEAR, W. & PARK, G. R. Bowel sounds during artificial ventilation, 668 (c)
MANARA, A. R. *see* PARK, G. R.
MANTZOURATOS, D. *see* ECONOMACOS, G.
MARTIN, B. C. *see* MADEJ, T. H.
MARTIN, D. G. Leak detection with a capnograph, 1025 (c)
MARTIN, R. & DUMAIS, R. Improving the success rate of axillary block, 1117 (c)
MARTYN, J. A. J. & GOLDHILL, D. R. Cold injury and hyperkalaemia, 561 (c)
MARTYN, J. A. J. *see* GOLDHILL, D. R.
MARYNIAK, J. K., HENDERSON, A. M., WOODALL, N. M., LIM, M. & SIMPSON, J. C. Beta-adrenoceptor blockade and suxamethonium-induced rise in plasma potassium, 71 (f)
MASON, D. F. *see* LINDSAY, S. L.
MASON, D. G. & WARK, K. J. Unexpected difficult intubation. Asymptomatic epiglottic cysts as a cause of upper airway obstruction during anaesthesia, 407
MASON, D. G., EDMONDSON, L. & MCHUGH, P. Fixation of epidural catheters, 672 (c)
MASON, R. A. The pulse oximeter—an early warning device?, 784 (c)
MATHER, S. J. Ondine's curse and the anaesthetist, 394
MATHIAS, J. A. & LUNN, J. N. Minimal monitoring and vigilance: editorial, 683
MAVER, E. *see* VONWILLER, J. B.
MAYALL, R. *see* KAY, B.
MAZZE, R. I. Nitrous oxide and pregnancy: a reply, 428 (c)
MEAKIN, G. & REMINGTON, S. Nebulised adrenaline: a reply, 322 (c)
MEHTA, S. Difficult extubation due to a kinked pilot tube, 443 (c)
MEHTA, S. Nasotracheal intubation: another approach, 1126 (c)

MEHTA, Y. & HOLE, P. Suxamethonium apnoea in a 4-month-old twin, 868
MEIKLEJOHN, B. H. The effect of rotation of an epidural needle. An *in vitro* study, 1180
MEIKLEJOHN, B. H., SMITH, G., ELLING, A. E. & HINDOCHA, N. Arterial oxygen desaturation during postoperative transportation: the influence of operation site, 1313 (f)
MEKKI, M. O. *see* CHANNA, A. B.
MENDEL, L. *see* PARK, G. R.
MENDEL, L. *see* SHELLY, M. P.
MILASZKIEWICZ, R. *see* SHARPE, E.
MILES, J. M. & THOMPSON, G. R. Treatment of severe accidental hypothermia using the Clinitron bed, 415
MILES, J. M. & THOMPSON, G. R. Treatment of accidental hypothermia with the Clinitron bed: a reply, 1122 (c)
MILLAR, J. M. & HALL, P. J. Nausea and vomiting after prostaglandins in day case termination of pregnancy. The efficacy of low dose droperiodol, 613
MILLAR, S. W. Unexpected difficult intubation, 1021 (c)
MILLER, C. D. & DOUGALL, J. R. Resistance to cardioplegia, 1117 (c)
MILLIGAN, K. R., HOWARD, R. C. & DUNDEE, J. W. The effect of benzodiazepines on evoked potentials, 1237 (c)
MILLIGAN, K. R. *see* FURNESS, G.
MILLIGAN, K. R. *see* O'TOOLE, D. P.
MILNE, A. C. *see* JENKINS, J.
MILTON, J. *see* RAILTON, R.
MIMPRISS, T. J. *see* SEKAR, M.
MIRAKHUR, R. K. & JONES, C. J. Ventilation and the oculocardiac reflex: a reply, 325 (c)
MIRAKHUR, R. K., SHEPHERD, W. F. I., LAVERY, G. G. & ELLIOTT, P. The effects of vecuronium on intra-ocular pressure, 944
MITCHELL, M. D. & DOWNING, J. W. Cardiovascular collapse following epidural anaesthesia for Caesarean section, 1228 (c)
MITSUKURI, S. *see* DE GROOD, P. M. R. M.
MOFTI, A. B. *see* CHANNA, A. B.
MOGHRABI, R. *see* BARAKA, A.
MOHANDAS, K. *see* PARSONS, R. S.
MOIR, D. D. *see* THORNBURN, J.
MOKRISKI, B. L. K. *see* MALINOW, A. M.
MONTGOMERY, J. N. *see* DUTHIE, D. J. R.
MOORE, A. P. *see* MOORE, J. K.
MOORE, J. *see* WILSON, C. M.
MOORE, J. K. & MOORE, A. P. Postoperative complications of dystrophia myotonica, 529
MOORE, J. K. & MOORE, A. P. Postoperative complications of dystrophia myotonica: a reply, 1024 (c)
MORGAN, B. A., PERKS, D., CONACHER, I. D. & PAES, M. L. Combined unilateral high frequency jet ventilation and contralateral intermittent positive pressure ventilation, 975
MORGAN, B. M. *see* LAISHLEY, R. S.
MORGAN, G. *see* MORRISON, P.
MORGAN, M. *see* GROUNDS, R. M.
MORI, K. The EEG and awareness during anaesthesia: editorial, 1153
MORLEY, S. J. *see* JACK, T. M.
MORRISON, C. E., DUTTON, D., HOWIE, H. & GILMOUR, H. Pethidine compared with meptazinol during labour. A prospective randomised double-blind study in 1100 patients, 7
MORRISON, P. & MORGAN, G. Removal of a giant ovarian cyst. Anaesthetic and intensive care management, 965
MORRITT, G. N. *see* CONACHER, I. D.
MOSELEY, H., KUMAR, A. Y., SHANKAR, K. B. & RAO, P. S. Air–oxygen mixtures, 1336 (c)
MOSELEY, H., KUMAR, A. Y., SHANKAR, K. B., RAO, P. S. & HOMI, J. Should air–oxygen replace nitrous oxide–oxygen in general anaesthesia?, 609
MOSELEY, H. *see* SHANKAR, K. B.
MOSKOVITS, P. E., RICHES, P. & SONI, N. A red patient: immunological reaction to glycine?, 962
MOSTAFA, S. M. Complications of difficult intubation, 1241 (c)
MOSTAFA, S. M. Training in fibreoptic techniques, 429 (c)
MOSTAFA, S. M. & LOCKHART, A. Vomiting following ophthalmic anaesthesia: a reply, 897 (c)
MOUSDALE, S. *see* DUMONT, S. M.
MOWBRAY, A., WONG, K. K. S. & MURRAY, J. M. Intercostal catheterisation. An alternative approach to the paravertebral space, 958
MOWBRAY, A. *see* MURRAY, J. M.
MUNDY, J. V. B. *see* WRIGHT, P. J.
MURAT, I., CHAUSSAIN, M., HAMZA, J. & SAINT-MAURICE, CL. The respiratory effects of isoflurane, enflurane and halothane in spontaneously breathing children, 711
MURDAY, A. *see* SHERRY, K. M.
MURRAY, J. M. & MOWBRAY, A. Local tissue oxygenation following radial artery cannulation, 1070
MURRAY, J. M. *see* MOWBRAY, A.

MURRAY-WILSON, A. *see* COOPER, C. M. S.

NANULESCU, M. *see* CARDAN, E.
NASH, D. G. *see* KONARZEWSKI, W. H.
NEGRUTIU, S. *see* CARDAN, E.
NEWCOMBE, G. N. Serological markers for hepatitis B, 1239 (c)
NEWMAN, B. Cardiopulmonary resuscitation in district general hospitals, 314 (c)
NEWMAN, L. H., MCDONALD, J. C., WALLACE, P. G. M. & LEDINGHAM, I. MCA. Propofol infusion for sedation in intensive care, 929
NICKALLS, R. W. D. A new percutaneous infraclavicular approach to the axillary vein, 151
NIELSEN, J. W. *see* HØGSKILDE, S.
NIMMO, W. S. *see* DUTHIE, D. J. R.
NIMMO, W. S. *see* OWEN, H.
NOLAN, D. *see* KAY, B.
NORLEY, I. Erroneous actuation of the pulse oximeter, 1116 (c)
NORLEY, I. Loading frame for pneumatic pressure infusor, 566 (c)
NORMAN, J. *see* BOWEN, D. J.
NORMANDALE, J., PATRICK, M., SHERRY, K. M. & FENECK, R. O. Comparison of conventional intermittent positive pressure ventilation with high frequency jet ventilation. Studies following aortocoronary bypass graft surgery, 824
NOTT, M. R. Drilled for safety, 563 (c)
NOTT, M. R. Patients with problems, 328 (c)
NUMMINEN, M. K. *see* TUOMINEN, M. K.
NUNN, G. A new laryngoscope. A modified laryngoscope to facilitate intubation in cases of restricted access, 877
NUNN, J. F. Nitrous oxide and pregnancy, 427 (c)

OATES, P. D. *see* ALSTON, R. P.
O'CONNELL, P. *see* SMITH, D. C.
O'CONNOR, S. A. & WILKINSON, D. J. Relative potency of propofol and thiopentone, 318 (c)
O'DEA, J. & HALL, I. Oesophageal stethoscope, 1337 (c)
OGDEN, B. *see* HANNING, C. D.
OKELL, R. W. & SPRIGGE, J. S. Unintentional dural puncture. A survey of recognition and management, 1110 (f)
OLSSON, S.-G. Humidifier-induced hypercarbia: a reply, 673 (c)
ORLIKOWSKI, C. *see* GREBENIK, C. R.
OSWAL, V. H. *see* HUNTON, J.
O'TOOLE, D. P., MILLIGAN, K.R., HOWE, J. P., MCCOLLUM, J.S.C. & DUNDEE, J. W. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia, 373
OWEN, B. Protocols in obstetric units: their use in Wales in 1983, 1323 (f)
OWEN, B. The anaesthetist and Maternity Services Liaison Committees, 894 (c)
OWEN, H., GAUKROGER, P. B., CHERRY, D. A. & GOURLAY, G. K. AIDS and anaesthesia, 430 (c)
OWEN, H., REEKIE, R. M., CLEMENTS, J. A., WATSON, R. & NIMMO, W. S. Analgesia from morphine and ketamine. A comparison of infusions of morphine and ketamine for postoperative analgesia, 1051

PAES, M. L. *see* CONACHER, I. D.
PAES, M. L. *see* MORGAN, B. A.
PARK, G. R., MANARA, A. R., MENDEL, L. & BATEMAN, P. E. Ketamine infusion. Its use as a sedative, inotrope and bronchodilator in a critically ill patient, 980
PARK, G. R. *see* MANARA, A. R.
PARK, G. R. *see* SHELLY, M. P.
PARK, R. J. *see* POLSON, R. J.
PARRY, P. *see* HANNING, C. D.
PARSONS, R. S., WETZEL, R. C. & MOHANDAS, K. The acute effects of intravenous isosorbide dinitrate during cardiac surgery, 498
PATEL, D. *see* SALE, J. P.
PATRICK, M. *see* NORMANDALE, J.
PAUL, D. L. An antipollution device for use with the Jackson–Rees modification of Ayre's T-piece, 439 (c)
PAUL, D. L. & MCKEEOWN, D. W. Supine faints, 1121 (c)
PAULL, J. D. & FORTUNE, D. W. Hepatotoxicity and death following two enflurane anaesthetics, 1191
PAYNE-JAMES, J. J., REES, G. R. & SILK D. B. A. Bowel sounds, 893 (c)
PEARCE, F. L. *see* WITHINGTON, D. E.
PELIMON, A. & SIMUNOVIC, Z. Modified Magill forceps for difficult tracheal intubation, 83 (c)
PENNANT, J. H. *see* GOLDSTONE, J. C.
PEREIRA, N. H. *see* REID, M. F.
PERERA, S. *see* CHARTERS, P.
PERKS, D. *see* MORGAN, B. A.

PERKS, D. *see* PRINCE, G. D.
PETHYBRIDGE, R. J. *see* TIGHE, S. Q. M.
PHILIP, B. K. & PHILIP, J. H. Pressure–flow relationships in intravenous infusion systems, 775 (c)
PHILIP, J. H. *see* PHILIP B. K.
PHILLIPS, A. J. & SPENCE, A. A. Zidovudine and the anaesthetist: editorial, 799
PHILLIPS, B. *see* COLEMAN, P.
PHILLIPS, D. C. & MACDONALD, R. Epidural catheter migration during labour, 661 (f)
PHILLIPS, P. D. *see* REID, M. F.
PILLAI, R. *see* SMITH, D. C.
PINNOCK, C. A. & FELL, D. Triazolam premedication, 316 (c)
PITHER, C. *see* RICE, A. S. C.
PITKÄNEN, M. T. *see* TUOMINEN, M. K.
PLATT, M. & WHITE, D. C. Calories in sedation, 322 (c)
PLENDERLEITH, J. L. A new ventilator for closed breathing systems, 1335 (c)
POLSON, R. J., PARKS, G. R., LINDOP, M. J., FARMAN, J. V., COLNE, R. Y. & WILLIAMS, R. The prevention of renal impairment in patients undergoing orthotopic liver grafting by infusion of low dose dopamine, 15
POP, R. *see* CARDAN, E.
PORTEOUS, R. Pain-free intravenous injections, 1021 (c)
POUTTU, J. *see* COZANITIS, D. A.
POWERS, K. M. & ARTRU, A. A. Nitrous oxide does not alter oxyhaemoglobin dissociation in dog or man, 668 (c)
PRINCE, G. D., PERKS, D. & FRASER, G. Difficulties with tracheal suction, 84 (c)
PROCTER, A. J. M. *see* HOLLIS, N.
PULGAR, S. *see* SOLARES, G.
PURCELL-JONES, G., DORMON, F. & SUMNER, E. The use of opioids in neonates. A retrospective study of 933 cases, 1316 (f)
PURCELL-JONES, G., SPEEDY, H. M. & JUSTINS, D. M. Upper limb sympathetic blockage following intercostal nerve blocks, 984
PURI, G. D. Arterial to end tidal carbon dioxide tension difference during anaesthesia for tubal ligation, 1338 (c)
PURI, G. D., GEORGE, M. A., SINGH, H. & BATRA, Y. K. Awareness under anaesthesia due to a defective gas-loaded regulator, 539
PUSEY, J. M., CHARLTON, S. M., SKINNER, J. B. & ASSEM, E. S. K. Anaphylactoid reaction to alcuronium, 164

RADFORD, S. G. *see* SIMPSON, P. J.
RAILTON, R., MILTON, J. & DAVIE, R. A. Is your scavenging working?, 86 (c)
RAITT, D. G. *see* BRICKER, S. R. W.
RAJU, R. Humidifier-induced hypercarbia, 672 (c)
RAMAGE, D. T. O. *see* FORREST, T.
RAMASAMY, M. *see* SHANKAR, K. B.
RAMOS, F. *see* SOLARES, G.
RAO, P. S. *see* MOSELEY, H.
RAO, U., CAMPBELL, I. T., SUTHERST, J. R. & CATLEY, D. M. Epidural meptazinol, 218 (c)
RAVALIA, A. & STOCKWELL, M. A. Displacement of a minitracheotomy tube during high frequency jet ventilation, 1306
RAVNBORG, M. *see* JENSEN, F. M.
RAYBOULD, D. & BRADSHAW, E. G. Premedication for day case surgery. A study of oral midazolam, 591
READ, M. S. Anaesthesia and the subclavian steal syndrome, 442 (c)
REEKIE, R. M. *see* OWEN, H.
REES, J. L. *see* GROVES, N. D.
REES, R. G. *see* PAYNE-JAMES, J. J.
REID, M. F., HARRIS, R., PHILLIPS, P. D., BARKER, I., PEREIRA, N. H. & BENNETT, N. R. Day case herniotomy in children. A comparison of ilio-inguinal nerve block and wound infiltration for postoperative analgesia, 658 (f)
REMINGTON, S. *see* MEAKIN, G.
REPLYUK, J. Heat and moisture exchangers, 1120 (c)
REYNOLDS, F. Auto-antagonism of buprenorphine, 1334 (c)
REYNOLDS, F. Caudal epidural—possible subdural spread?, 440 (c)
REYNOLDS, F. *see* LAISHLEY, R. S.
REYNOLDS, F. *see* RICE, A. S. C.
RICE, A. S. C. & PITHER, C. Nerve blocks for hip surgery, 1016 (c)
RICE, A. S. C. & REYNOLDS, F. Comparison of trichloroethylene and enflurane as adjuncts to nitrous oxide and relaxant anaesthesia, 1320 (f)
RICHARDS, G. *see* KONARZEWSKI, W. H.
RICHARDS, M. Miller's syndrome. Anaesthetic management of postaxial acrofacial dysostosis, 871
RICHARDSON, J. Propofol infusion for coronary artery bypass surgery in a patient with a suspected malignant hyperpyrexia, 1125 (c)
RICHARDSON, J. C. *see* RUSSELL, G. N.

RICHES, P. *see* MOSKOVITS, P. E.
RICKFORD, W. J. K. *see* MALINOW, A. M.
RIMMER, M. E. *see* ALLEN S. C.
ROBINSON, J. M. *see* YOUNG, P. N.
ROBERTS, P. J. Unattached inner coaxial tube, 1128 (c)
ROBSON, N. J. Carminative property of peppermint in magnesium trisilicate mixture, BP, 776 (c)
ROCKE, D. A. *see* MACGILLIVRAY, R. G.
RODT, S. *see* FLAATTEN, H.
ROE, P. G., TYLER, C. K. G. & BARNES, P. K. Evaluation of oxygen analysers; a reply, 1127 (c)
ROE, P. G., TYLER, C. K. G., TENNANT, R. & BARNES, P. K. Oxygen analysers. An evaluation of five fuel cell models, 175
ROGERS, H. *see* LOUGHNAN, B. L.
ROLLY, G. *see* DONADONI, R.
ROLLY, G. *see* HERREGODS, L.
ROSEN, M. Future organisation of anaesthetic health care: editorial, 1043
ROSEN, M. *see* GROVES, N. D.
ROSEN, M. *see* JONES, R. M.
ROSEN, M. *see* YUKIOKA, H.
ROSENBERG, P. H. *see* COZANITIS, D. A.
ROSENBERG, P. H. *see* TUOMINEN, M. K.
ROSLAND, J. *see* FLAATTEN, H.
ROSS, D. G. Kinked tube or bronchospasm?, 441 (c)
ROSSEEL, M. T. *see* HERREGODS, L.
ROTMAN, H. *see* HODSMAN, N. B. A.
ROY, R. C., CARTER, R. F. & WRIGHT, P. D. Somatostatin, anaesthesia, and the carcinoid syndrome. Peri-operative administration of a somatostatin analogue to suppress carcinoid tumour activity, 627
RUBIN, A. P. *see* EWART, M. C.
RUIZ, K., STEVENS, J. D., TRAIN, J. J. A. & WATKINS, J. Anaphylactoid reactions to prilocaine, 1078
RUNCIMAN, W. B., ILSLEY, A. H., CARAPETIS, R. J., SELBY, D. G. & RYALL, R. G. Nitrous oxide and oxyhaemoglobin dissociation, 894 (c)
RUSSELL, G. N., FRAZER, S. & RICHARDSON, J. C. Difficult tracheal intubation, 82 (c)
RUSSELL, G. N., SMITH, C. L., SNOWDON, S. L. & BRYSON, T. H. L. Pre-oxygenation and the parturient patient, 346
RUTHERFORD, C. F. *see* LOUGHNAN, B. L.
RUTTEN, J. M. J. *see* DE GROOD, P. M. R. M.
RUTTER, G. G. R., AVELING, W. & TUSIEWICZ, K. The respiratory depressant effects of nalbuphine and papaveretum as intramuscular premedication, 1176
RYALL, R. G. *see* RUNCIMAN, W. B.
RYAN, D. W. *see* WAGSTAFF, A.
RYE, J. G. SI units, Newtons and apples, 1025 (c)

SABO, B. A. *see* GILBERT, J.
SADDLER, J. M. & HORSEY, P. J. The new generation gelatins. A review of their history, manufacture and properties, 998
SAGGU, G. S. *see* YUKIOKA, H.
SAINT-MAURICE, CL. *see* MURAT, I.
SALE, J. P., PATEL, D., DUNCAN, B. & WATERS, J. H. Anaesthesia for combined heart and lung transplantation, 249
SALEM, M. G. D. Low dose infusion of dopamine, 572 (c)
SALLER, D. N. *see* MALINOW, A. M.
SAMSOON, G. L. T. & YOUNG, J. R. B. Difficult tracheal intubation: a retrospective study, 487
SAMUEL, J. R. *see* ABBOTT, M. A.
SANGALA, W. & DIXON, J. Pancuronium and renal failure, 1236 (c)
SANSOME, A. J. A difficult nasal intubation, 209 (c)
SAPSFORD, D. J. & BUSH, G. H. Prolonged neuromuscular blockade in a patient with a normal genotype: a reply, 214 (c)
SAUNDERS, D. A. *see* BOWEN, D. J.
SCADDING, G. K. *see* WITHINGTON, D. E.
SCHACHTER, M. *see* HILL, H.
SCOTT, R. P. F. & CHAPMAN, I. A problem with the Argyll tracheal tube, 1123 (c)
SEARLE, J. F. *see* WILLATTS, S. M.
SEBEL, P. S. The effect of benzodiazepines on evoked potentials, 1237 (c)
SEBEL, P. S. *see* LOUGHNAN, B. L.
SECHER, O. Early textbooks on anaesthesia, 1022 (c)
SEE, T. Y. *see* KWAN, J. Y.
SEKAR, M. & MIMPRISS, T. J. Buprenorphine, benzodiazepines and prolonged respiratory depression, 567 (c)
SELBY, D. G. *see* RUNCIMAN, W. B.
SELLERS, W. F. S. & YOGENDRAN, S. Difficult tracheal intubation, 1243 (c)

SEVER, P. S. *see* HILL, H.
SEVERN, A. M. Epidural block for elective Caesarean section, 435 (c)
SEYMOUR, L. *see* JONES, R. M.
SHAH, J. L. Caudal epidurals—a further caution, 440 (c)
SHAH, J. L. Epidural block for Caesarean section, 327 (c)
SHAH, M. V. *see* GOLDMANN, L.
SHANKAR, K. B. Deviations from international standards, 444 (c)
SHANKAR, K. B. High frequency jet ventilation and arterial to end-tidal CO_2 difference, 1124 (c)
SHANKAR, K. B., MOSELEY, H., KUMAR, Y. & RAMASAMY, M. Bain anaesthetic system, gender and obesity index, 779 (c)
SHANKAR, K. B., MOSELEY, H., KUMAR, Y. & VEMULA, V. Arterial to end tidal CO_2 tension differences: a reply, 211 (c)
SHANKAR, K. B., MOSELEY, H., KUMAR, Y., VEMULA, V. & KRISHNAN, A. Arterial to end-tidal carbon dioxide tension difference during anaesthesia for tubal ligation, 482
SHANKAR, K. B., MOSELEY, H., KUMAR, Y., VEMULA, V. & KRISHNAN, A. Arterial to end-tidal carbon dioxide tension difference during anaesthesia for tubal ligation: a reply, 1338 (c)
SHANKAR, K. B. *see* MOSELEY, H.
SHARMA, S. *see* GROVER, V. K.
SHARPE, E., MILASZKIEWICZ, R. & CARLI, F. A case of prolonged hypotension following intravenous guanethidine block, 1081
SHEARER, E. S. & WENSTONE, R. Bradycardia during elevation of zygomatic fractures. A variation of the oculocardiac reflex, 1207
SHEIKH, M. H. *see* CHANNA, A. B.
SHELLY, M. P. Bowel sounds during intermittent positive pressure ventilation, 207 (c)
SHELLY, M. P. & PARK, G. R. Intercostal nerve blockade for children, 541 (f)
SHELLY, M. P., MENDEL, & PARK, G. R. Failure of critically ill patients to metabolise midazolam, 619
SHEPHERD, W. F. I. *see* MIRAKHUR, R. K.
SHERLOCK, D. A. & MCNICOL, L. R. Anaesthesia and septo-optic dysplasia. Implications of missed diagnosis in the peri-operative period, 1302
SHERRY, K. M. & MURDAY, A. A nasal adhesion following nasotracheal intubation, 651
SHERRY, K. M., KEELING, P. A., JONES, H. M. & AVELING, W. Insertion of intratracheal stents. Anaesthetic management using high frequency jet ventilation or cardiopulmonary bypass, 61
SHERRY, K. M., WINDSOR, J. P. W. & FENECK, R. O. Comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation, 1276
SHERRY, K. M. *see* NORMANDALE, J.
SHEVDE, K. *see* CHERALA, S.
SHIMADA, Y. *see* KAINUMA, M.
SIDES, C. A. Hypertension during anaesthesia with monoamine oxidase inhibitors, 633
SILK, D. B. A. *see* PAYNE-JAMES, J. J.
SIM, P. Preferential oxygen leak—an unusual case, 1330 (c)
SIMPSON, D. L. Beta blockade and nitroprusside: a reply, 1023 (c)
SIMPSON, D. L., MACRAE, W. R., WILDSMITH, J. A. W. & DALE, B. A. B. Acute beta-adrenoreceptor blockade and induced hypotension, 243
SIMPSON, E. *see* THORP, J. M.
SIMPSON, J. C. *see* MARYNIAK, J. K.
SIMPSON, K. H., CHATER, S. N. & SWINDELLS, S. R. Oxgenation during electroconvulsive therapy, 1234 (c)
SIMPSON, K. H. *see* CHATER, S. N.
SIMPSON, P. J., RADFORD, S. G. & LOCKYER, J. A. The influence of anaesthesia on the acute phase protein response to surgery, 690
SIMUNOVIC, Z. *see* PELIMON, A.
SINCLAIR, J. F., MALCOLM, G. A., STEPHENSON, J. B. P. & HALWORTH, D. Prolonged neuromuscular blockade in an infant, 1020 (c)
SINCLAIR, J. R. *see* WILSON, I. H.
SINCLAIR, M. E., ASHBY, M. W. & KURTZ, J. B. The prevalence of serological markers for hepatitis B virus infection amongst anaesthetists in the Oxford region, 30
SINGH, H. *see* GROVER, V. K.
SINGH, H. *see* PURI, G. D.
SKINNER, A. C. Difficult bronchial intubation, 567 (c)
SKINNER, J. B. *see* PUSEY, J. M.
SLEIGH, J. W. *see* STUART-TAYLOR, M. E.
SMITH, B. Broken control on a Selectatec vaporizer: a reply, 215 (c)
SMITH, B. *see* DRAKE, H. F.
SMITH, B. E. & ALLISON, A. Nerve blocks for hip surgery: a reply, 1016 (c)
SMITH, B. E. & ALLISON, A. Use of a low-power nerve stimulator during sciatic nerve block, 296
SMITH, C. L. & SNOWDON, S. L. Anaesthesia and glucose-6-phosphate dehydrogenase deficiency. A case report and review of the literature, 281

SMITH, C. L., HUNTER, J. M. & JONES, R. S. Prolonged paralysis following an infusion of alcuronium in a patient with renal dysfunction, 522
SMITH, C. L., HUNTER, J. M. & JONES, R. S. Vecuronium infusions in patients with renal failure in an ITU, 387
SMITH, C. L. *see* RUSSELL, G. N.
SMITH, D. C. & O'CONNELL, P. The influence of premedication on the occurrence of dysrhythmias during oral surgery, 882 (f)
SMITH, D. C., PILLAI, R. & GILLBE, C. E. Tracheopathia osteochondroplastica. A cause of unexpected difficulty in tracheal intubation, 536
SMITH, G. *see* MEIKLEJOHN, B. H.
SMITH, G. B., GUSBERG, R. J., JORDAN, R. H. & KIM, B. Histamine levels and cardiovascular responses during splenectomy and splenorenal shunt formation in a patient with systemic mastocytosis, 861
SMITH, M. F. *see* LINDOP, M. J.
SMITH, T. G. C. *see* ALLEN, S. C.
SNEYD, J. R. Consent for epidural analgesia, 1232 (c)
SNEYD, R. Oxgenation during electroconvulsive therapy, 431 (c)
SNOWDON, S. L. *see* RUSSELL, G. N.
SNOWDON, S. L. *see* SMITH, C. L.
SOLARES, G., BLANCO, E., PULGAR, S., DIAGO, C. & RAMOS, F. Carcinoid syndrome and intravenous cyproheptadine, 989
SOLARES, G., RAMOS, F., BLANCO, J. & BLANCO, E. Alcuronium, pancuronium and phaeochromocytoma, 77 (c)
SOLD, M. J. & WEIS, K. H. If nothing goes wrong—is everything alright?, 557 (c)
SONI, N. & LEE, K. G. AIDS and anaesthesia: a reply, 431 (c)
SONI, N. *see* MOSKOVITS, P. E.
SØRENSEN, M. B. *see* HØGSKILDE, S.
SOSIS, M. Limitations of the Grass FT03 transducer, 85 (c)
SPARGO, P. M., APADOO, A. & WILTON, H. J. An improved antipollution device for the Jackson–Rees modification of the Ayre's T-piece, 1240 (c)
SPARLING, R. *see* WAGSTAFF, A.
SPEEDY, H. M. *see* PURCELL-JONES, G.
SPENCE, A. A. *see* DUTHIE, D. J. R.
SPENCE, A. A. *see* PHILLIPS, A. J.
SPRAGUE, N. B. & ARCHER, P. L. Magill versus Mallinckrodt tracheal tubes. A comparative study of postoperative sore throat, 306 (f)
SPRIGGE, J. S. *see* OKELL, R. W.
STAFFORD, L. B. *see* FRANK, M.
STANDEN, P. J., HAIN, W. R. & HOSKER, K. J. Retention of auditory information presented during anaesthesia. A study of children who received light general anaesthesia, 604
STEPHENSON, J. B. P. *see* SINCLAIR, J. F.
STEVENS, J. D. *see* RUIZ, K.
STOCKWELL, M. A. *see* RAVALIA, A.
STODDART, J. C. A way forward for intensive care: a reply, 552 (c)
STODDART, J. C. Benefits of pulmonary artery catheterisation: a reply, 436 (c)
STOKES, D. N. Re-insertion of minitracheotomy, 782 (c)
STRANGEWAYS, J. E. M. *see* ALLT-GRAHAM, J.
STRANGEWAYS, J. E. M. *see* GALLAGHER, J.
STRUBE, P. J., HULANDS, G. H. & HALSEY, M. J. Serum fluoride levels in morbidly obese patients: enflurane compared with isoflurane anaesthesia, 685
STRUNIN, L. & DAVIES, J. M. Use of volatile anaesthetics in the New World, 774 (c)
STRUNIN, L. *see* MADEJ, T. H.
STUART-TAYLOR, M. E. & SLEIGH, J. W. Alfentanil infusions. Comparison of bolus administration of fentanyl with three alfentanil infusion regimens, 1218 (f)
SUGDEN, J. C. & BEMBRIDGE, J. L. A contaminated Marcain ampoule, 87 (c)
SUGDEN, J. C. *see* CHATER, S. N.
SUM PING, J. S. T. *see* KAY, B.
SUMNER, E. *see* HENDERSON, A. M.
SUMNER, E. *see* PURCELL-JONES, G.
SUTHERST, J. R. *see* RAO, U.
SWAINE, C. N. *see* EASON, J. R.
SWINDELLS, S. R. *see* SIMPSON, K. H.
SYMONS, I. E. Smoking and anaesthesia, 569 (c)
SYNNOTT, A., WREN, W. S. & DAVENPORT, J. Intratracheal pressure during controlled ventilation in infants, 1333 (c)
SYNNOT, A., WREN, W. S. & DAVENPORT, J. Peak intratracheal pressure during controlled ventilation in infants and children. A computer study of the Servo 900C ventilator, 719

TACKLEY, R. M. & TREGASKIS, B. Fatal disseminated intravascular coagulation following a monoamine oxidase inhibitor/tricyclic interaction, 760
TANSKI, J. & JAMES, R. H. Kinked pilot tube, 1022 (c)
TAYLOR, D. *see* DEAR, G. DE L.
TAYLOR, G. W. *see* CHANNA, A. B.
TAYLOR, M. B. Erroneous actuation of the pulse oximeter: a reply, 1116 (c)
TAYLOR, M. B., WHITWAM, J. G. & WORSLEY, A. Paroxysmal nocturnal haemoglobinuria. Peri-operative management of a patient with Budd–Chiari syndrome, 639
TAYLOR, M. B. *see* GROUNDS, R. M.
TENNANT, R. *see* ROE, P. G.
TEY, H. K. *see* MACLEOD, D. M.
THEEMAN, M. *see* WARRAN, P.
THOMAS, D. *see* LOUGHNAN, B. L.
THOMAS, D. *see* TIPPING, T.
THOMAS, D. G. *see* LINDOP, M. J.
THOMAS, D. V. A traumatic nastotracheal intubation, 573 (c)
THOMAS, J. *see* CALLANDER, C. C.
THOMAS, V. L. *see* WILTON, N. C. T.
THOMPSON, G. *see* MILES, J.
THOMPSON, S. *see* KONARZEWSKI, W. H.
THOMSON, S. J. & YATE, P. M. Bradycardia after propofol infusion, 430 (c)
THORBURN, J. & MOIR, D. D. Antacid therapy for emergency Caesarean section, 352
THORNILY, A. *see* HUNTER, D. N.
THORP, J. M. Pleural aspiration with a central venous catheter, 896 (c)
THORP, J. M. & HIGGINS, M. Non vagolytic anaesthetic sequence—sinus arrest, 432 (c)
THORP, J. M., MACKENZIE, I. & SIMPSON, E. Gross hypernatraemia associated with the use of antiseptic surgical packs, 750
THORP, J. M., MACKENZIE, I. & SIMPSON, E. Gross hypernatraemia associated with the use of antiseptic surgical packs: a reply, 1331 (c)
THURLOW, A. C. *see* VAN BESOUW, J. P.
TIGHE, S. Q. M. & PETHYBRIDGE, R. J. A comparison of halothane and trichloroethylene with isoflurane. A study of drawover air anaesthesia with the Triservice anaesthetic apparatus, 887 (f)
TIPPING, T., BLOGG, C. E. & THOMAS, D. Triazolam premedication: a reply, 316 (c)
TOYODA, Y. *see* KUBOTA, Y.
TRAIN, J. J. A. *see* RUIZ, K.
TRAN, Y. & HEDLEY, R. Misplacement of a minitracheotomy tube, 783 (c)
TREASURE, T. *see* DRAKE, H. F.
TREFFERS, R. & DE LANGE, J. J. Accidental subdural catheterisation, 556 (c)
TREGASKIS, B. *see* TACKLEY, R. M.
TSUNETO, S. *see* YAMASHITA, M.
TUNSTALL, M. E. *see* MACLEOD, D. M.
TUOMINEN, M. K. & ROSENBERG, P. H. Quality of axillary brachial plexus block: a reply, 775 (c)
TUOMINEN, M. K., PITKÄNEN, M. T., NUMMINEN, M. K. & ROSENBERG, P. H. Quality of axillary brachial plexus block. Comparison of success rate using perivascular and nerve stimulator techniques, 20
TURNER, D. A. B. & WRIGHT, E. M. Efficiency of heat and moisture exchangers, 1117 (c)
TURNER, D. A. B. *see* BLOOR, G. K.
TUSIEWICZ, K. *see* RUTTER, G. G. R.
TWEEDIE, I. E. Intravenous injections, 1339 (c)
TWIGLEY, A., CHAKRABARTI, M. K. & WHITWAM, J. G. A new ventilator for closed breathing systems, 419
TWIGLEY, A., CHAKRABARTI, M. K. & WHITWAM, J. G. A new ventilator for closed breathing systems: a reply, 1335 (c)
TWIGLEY, A., CHAKRABARTI, M. K. & WHITWAM, J. G. Nomenclature of circle absorption breathing systems: a reply, 1018 (c)
TWIGLEY, A. J. *see* ALLSOP, P.
TWYCROSS, R. G. *see* HANKS, G. W.
TYLER, C. K. G. *see* ROE, P. G.

UEDA, Y. *see* KUBOTA, Y.
UNDERHILL, S., BUSH, G. H. & HARPER, S. J. Lorazepam in a fast dissolving dose form as a premedicant for children, 319 (c)

VALLIS, C. J. *see* HENDERSON, A. M.
VAMNES, J. *see* FLAATTEN, H.
VAN BESOUW, J. P. A hazard of silencers for jet ventilators, 81 (c)
VAN BESOUW, J. P. & THURLOW, A. C. A hazard of free-standing vaporizers, 671 (c)
VANCE, I. P. Halothane and the Committee on Safety of Medicines, 212 (c)

VAN DEN BERG, A. A. Vomiting following ophthalmic anaesthesia, 897 (c)
VAN DEN BERG, A. A. & LAMBOURNE, A. Prochlorperazine and vomiting after eye surgery, 898 (c)
VAN DEN BERG, A. A., LAMBOURNE, A., YAZJI, N. S. & LAGHARI, N. A. Vomiting after ophthalmic surgery. Effects of intra-operative antiemetics and postoperative oral fluid restriction, 270
VAN DIEJEN, D., DRIESSEN, J. J. & KAANDERS, J. H. A. M. Spinal cord compression during chronic epidural morphine administration in a cancer patient, 1201
VAN EGMOND, J. *see* DE GROOD, P. M. R. M.
VAN LEEUWEN, L. *see* ZUURMOND, W. W. A.
VATASHSKY, E. & HASKEL, Y. The spasm of the sphincter of Oddi can be avoided, 564 (c)
VELLA, L. M. AIDS and anaesthesia, 573 (c)
VEMULA, V. *see* SHANKAR, K. B.
VERSICHELEN, L. *see* HERREGODS, L.
VONWILLER, J. B., LIBERMAN, H. & MAVER, E. Modified Magill forceps for difficult tracheal intubation, 777 (c)

WAGNER, J. *see* HØGSKILDE, S.
WAGSTAFF, A., SPARLING, R. & RYAN, D. W. Minitracheostomy, 216 (c)
WAINWRIGHT, A. P. & BRODRICK, P. M. Suxamethonium in myasthenia gravis, 950
WAIT, C. M. Identification of the epidural space, 1231 (c)
WAIT, C. M., GOAT, V. A. & BLOGG, C. E. Feedback control of neuromuscular blockade. A simple system for infusion of atracurium, 1212
WALDMANN, C. S. *see* ALLEN, S. C.
WALKER, V. A. *see* HANKS, G. W.
WALKER, V. A. *see* JACK, T. M.
WALLACE, P. G. M. *see* NEWMAN, L. H.
WANG, L. P., FOG, J. & BOVE, M. Transient hearing loss following spinal anaesthesia, 1258
WARK, K. J. *see* MASON, D. G.
WARRAN, P., THEEMAN, M., BOLD, A. M. & JONES, S. Hypercholinesterasaemia and suxamethonium resistance, 855
WATERS, J. H. *see* SALE, J. P.
WATKINS, J. *see* RUIZ, K.
WATSON, A. K. A contaminated Marcain ampoule: a reply, 87 (c)
WATSON, D. M. Postmortem removal of tracheal tube, 554 (c)
WATSON, N. C. *see* MADEJ, T. H.
WATSON, R. *see* OWEN, H.
WAUCHOB, T. D. Leasing of equipment, 219 (c)
WEAVER, J. S. *see* GILBERT, J.
WEBB, T. B. Nasal intubation, 329 (c)
WEBSTER, N. R. & COHEN, A. T. Closed-loop administration of atracurium. Steady-state neuromuscular blockade during surgery using a computer controlled closed-loop atracurium infusion, 1085
WEIS, K. H. *see* SOLD, M. J.
WELSH, B. E. Selective bronchial intubation, 82 (c)
WENGEN, D. F. À. Piriform fossa perforation during attempted tracheal intubation, 519
WENSTONE, R. *see* SHEARER, E. S.
WESTON, G. A. *see* CARTER, C. A.
WETZEL, R. C. *see* PARSONS, R. S.
WHITBURN, R. *see* HUNTER, D. N.
WHITE, D. C. Air–oxygen mixtures, 1336 (c)
WHITE, D. C. *see* PLATT, M.
WHITE, J. B. *see* HOLLIS, N.
WHITLOCK, J. E. & CALDER, I. Transillumination in fibreoptic intubation, 570 (c)
WHITWAM, J. G. Benzodiazepines: editorial, 1255
WHITWAM, J. G. *see* HARROP-GRIFFITHS, A. W.
WHITWAM, J. G. *see* TAYLOR, M. B.
WHITWAM, J. G. *see* TWIGLEY, A.
WILDSMITH, J. A. W. *see* SIMPSON, D. L.
WILKINS, R. G. & EDWARDS, J. D. Benefits of pulmonary artery catheterisation, 436 (c)
WILKINS, R. G. *see* DOW, A. A. C.
WILKINSON, D. J. *see* O'CONNOR, S. A.
WILKINSON, K. *see* CHARTERS, P.
WILLATTS, S. M. & SEARLE, J. F. A way forward for intensive care, 551 (c)
WILLIAMS, P. A. D. Children and explosive anaesthetics, 212 (c)
WILLIAMS, R. Halothane specific antibody, 444 (c)
WILLIAMS, R. *see* POLSON, R. J.
WILLIAMSON, R. Hypotensive anaesthesia for middle ear surgery, 669 (c)
WILLIS, B. A. Minitracheostomy—a modified procedure, 216 (c)

WILSON, C. M., DUNDEE, J. W., MOORE, J., HOWARD, P. J. & COLLIER, P. S. A comparison of the early pharmacokinetics of midazolam in pregnant and nonpregnant women, 1057
WILSON, G. Dr Geoffrey Kaye, MD (Melb), MBBS, FFARACS, FFARCS, DA (R.C.P. & S.), 1903–1986, 426 (c)
WILSON, I. H. & SINCLAIR, J. R. Anaesthesia in difficult circumstances, 443 (c)
WILSON, I. H. *see* GAYLARD, D. G.
WILSON, M. E. The unit of applied force, 86 (c)
WILTON, H. J. *see* SPARGO, P. M.
WILTON, N. C. T. & THOMAS, V. L. Rapid inhalation induction: a reply, 773 (c)
WINDSOR, J. P. W. *see* SHERRY, K. M.
WISE, C. C. Gross hypernatraemia associated with the use of antiseptic surgical packs, 1331 (c)
WISHAW, K. J. *see* FINFER, S. R.
WITHINGTON, D. E., LEUNG, K. B. P., BROMLEY, L., SCADDING, G. K. & PEARCE, F. L. Basophil histamine release. A study in allergy to suxamethonium, 850
WOLFF, J., CARL, P. & CRAWFORD, M. E. Epidural buprenorphine for postoperative analgesia: a reply, 80 (c)
WONG, K. K. S. *see* MOWBRAY, A.
WOOD, D. G. L. Error in labelling: a reply, 572 (c)
WOOD, D. W. Oxygenation during electroconvulsive therapy, 431
WOOD, P. Difficulty in extubation, 220 (c)
WOODALL, N. M. *see* MARYNIAK, J. K.
WOOLLAM, C. H. M. Another hazard with the Penlon off-line vaporizer mounting system, 781 (c)
WORSLEY, A. *see* TAYLOR, M. B.
WREN, W. S. *see* ALLEN, P.
WREN, W. S. *see* SYNNOTT, A.
WRIGHT, E. M. *see* TURNER, D. A. B.
WRIGHT, J. T. *see* GOROSZENIUK, T.
WRIGHT, P. D. *see* ROY, R. C.
WRIGHT, P. J. & MUNDY, J. V. B. Tracheal tubes in neuroanaesthesia. Nylon reinforced latex rubber tracheal tubes, 1012 (f)
WROBEL, J. *see* BURGESS, R.
WÜST, H. J. & BROMAGE, P. R. Delayed respiratory arrest after epidural hydromorphone, 404

YAMASHITA, M. & TSUNETO, S. Alcohol vapour and the Normac analyser, 209 (c)
YATE, P. M. *see* THOMSON, S. J.
YATES, A. P. *see* LINDAHL, S. G. E.
YAZIGI, A. *see* BARAKA, A.
YAZJI, N. S. *see* VAN DEN BERG, A. A.
YENTIS, S. M. A laryngoscope adaptor for difficult intubation, 764
YOGANATHAN, S. & HOUGHTON, I. T. Isoflurane in a drawover anaesthesia system, 1241 (c)
YOGANATHAN, S., JOHNSTON, I. G. & HOUGHTON, I. T. Reservoir volume in a drawover system, 1337 (c)
YOGENDRAN, S. *see* SELLERS, W. F. S.
YOUNG, E. *see* ALLEN, S. C.
YOUNG, J. R. B. Visibility of pharyngeal structures as a predictor of difficult intubation: a reply, 1115 (c)
YOUNG, J. R. B. *see* SAMSOON, G. L. T.
YOUNG, P. N. & ROBINSON, J. M. Cellulitis as a complication of difficult tracheal intubation, 569 (c)
YUKIOKA, H., ROSEN, M., EVANS, K. T., LEACH, K. G., HAYWARD, M. W. J. & SAGGU, G. S. Gastric emptying and small bowel transit times in volunteers after intravenous morphine and nalbuphine, 704

ZUCK, D. Postoperative complications of dystrophia myotonica, 1023 (c)
ZUURMOND, W. W. A., VAN LEEUWEN, L. & HELMERS, J. H. J. H. Recovery from propofol infusion as the main agent for outpatient arthroscopy. A comparison with isoflurane, 356

Subject Index, Volume 42 (1987)

Abdominal surgery, the morphine sparing effect of ketorolac tromethamine (Gillies *et al.*), 727
Abdominal surgery, the morphine sparing effects of diclofenac sodium following (Hodsman *et al.*), 1005 (f)
Abscess following cannulation of the radial artery (Lindsay, Kerridge & Collett), 654
Abscess, mediastinal; atriobronchial fistula, an unusual complication of intravenous feeding in the presence of (Graziotti), 669 (c)
Accidental hypothermia, treatment with the Clinitron bed (Lloyd: Miles & Thompson), 1121 (c)
Accidental intra-arterial injection of propofol (Chong & Davis), 781 (c)
Accidental subdural catheterisation (Treffers & de Lange: Lee & Dodd), 556 (c)

Acupuncture, traditional Chinese, antiemetic studies with; comparison of manual needling with electrical stimulation and commonly used antiemetics (Ghaly, Fitzpatrick & Dundee), 1108 (f)
Acute phase protein response to surgery, influence of anaesthesia on (Simpson, Radford & Lockyer), 690
Adrenaline, nebulised (Gwinnutt & Lord: Choudhry: Child: Meakin & Remington), 320 (c)
Adrenaline, nebulised, croup and preservatives (Hinton & Goss), 436 (c)
AIDS and anaesthesia (Luke & Cundy), 1242 (c)
AIDS and anaesthesia (Owen *et al.*: Soni & Lee), 431 (c)
AIDS and anaesthesia (Vella), 573 (c)
Air–oxygen, should it replace nitrous oxide–oxygen in general anaesthesia? (Moseley *et al.*), 609
Air–oxygen mixtures (White: Moseley *et al.*), 1336 (c)
Airway pressure, continuous, safety of a new system for (Clayton & Catling), 440 (c)
Airway pressure, positive, continuous, treatment for persistent pneumothorax (Elphinstone & Grant), 987
Airway, upper, obstruction during anaesthesia, asymptomatic epiglottic cysts as a cause of (Mason & Wark), 407
Airway, upper, obstruction in neurofibromatosis (Crozier), 1209
Airway, upper, obstruction, an unusual cause of (Aldridge), 1239 (c)
Alarms, ventilator, should they be compulsory? (Gilston), 667 (c)
Alcohol vapour and the Normac analyser (Yamashita & Tsuneto), 209 (c)
Alcuronium, anaphylactoid reaction to (Pusey *et al.*), 164
Alcuronium infusion in a patient with renal dysfunction, prolonged paralysis following (Smith, Hunter & Jones), 522
Alcuronium, pancuronium and phaeochromocytoma (Solares *et al.*), 77
Alcuronium pretreatment, effect on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Alfentanil infusions, comparison of bolus administration of fentanyl with three alfentanil infusion regimens (Stuart-Taylor & Sleigh), 1218 (f)
Alfentanil by intravenous infusion as long-term sedation in intensive care (Cohen & Kelly), 545 (f)
Allergy to suxamethonium; basophil histamine release (Withington *et al.*), 850
Alphaxolone/alphadolone anaesthetic properties, comparison with pregnanolone emulsion (Høgskilde *et al.*), 1045
Alternative medicine (Dundee, Lynas & Ghaly), 76 (c)
Alveolar bubble, bursting the: editorial (Hills), 467
Ampoule, Marcain, contaminated (Sugden & Bembridge: Watson), 87 (c)
Ampoules, contamination of (Kirkpatrick), 779 (c)
Amyloidosis, primary, and skin damage (Dixon), 218 (c)
Anaemia, acute, severe, in a Jehovah's Witness; survival without blood transfusion (Howell & Bamber), 44
Anaesthesia and AIDS (Luke & Cundy), 1242 (c)
Anaesthesia and AIDS (Owen *et al.*: Soni & Lee), 431 (c)
Anaesthesia and AIDS (Vella), 573 (c)
Anaesthesia in difficult circumstances (Wilson & Sinclair), 443 (c)
Anaesthesia, early textbooks (Secher), 1022 (c)
Anaesthesia and intra-ocular pressure in young children, a study of three different techniques of anaesthesia (Dear *et al.*), 259
Anaesthesia and smoking: editorial (Jones, Rosen & Seymour), 1
Anaesthesia and smoking (Symons), 569 (c)
Anaesthesia and smoking (Callander: McKechnie: Jones & Rosen), 770 (c)
Anaesthetic health care, future organisation: editorial (Rosen), 1043
Anaesthetic literature, 99, 221, 335, 450, 574, 674, 789, 903, 1029, 1136, 1246, 1340
Anaesthetic machines, potential leaks through open Rotameter valves and empty cylinder yokes (McQuillan & Jackson), 1308
Anaesthetics, volatile, use in the New World (Strunin & Davies), 774 (c)
Anaesthetists, health of: editorial (Harrington), 131
Anaesthetist and Maternity Services Liaison Committees (Owen), 894 (c)
Anaesthetists, morbidity and early retirement among (McNamee, Keen & Corkill), 133
Anaesthetists, morbidity and early retirement (Adams: Hutchinson: Keen & McNamee), 1024 (c)
Anaesthetists, obstetric, implications of lupus anticoagulant for (Malinow *et al.*), 1291
Anaesthetists and Ondine's curse (Mather), 394
Anaesthetists in the Oxford region, prevalence of serological markers for hepatitis B virus infection amongst (Sinclair, Ashby & Kurtz), 30
Anaesthetist and zidovudine: editorial (Phillips & Spence), 799
Analgesia, epidural, cervical, during carotid artery surgery (Campkin: Kainuma & Shimada), 437 (c)
Analgesia, epidural, consent for (Sneyd), 1232 (c)
Analgesia, intravenous regional, pneumatic tourniquet paralysis following (Larsen & Hommelgaard), 526
Analgesia for neonates (Gauntlett), 1328 (c)
Analgesia, obstetric, nalbuphine for; comparison of nalbuphine with pethidine for pain relief in labour when administered by patient-controlled analgesia (Frank *et al.*), 697
Analgesia, patient-controlled, feedback using a speech synthesiser (Hodsman *et al.*), 767 (f)

Analgesia, postoperative, in children following herniotomy and orchidopexy, comparison of two regional techniques (Cross & Barrett), 845

Analgesia, postoperative, a comparison of ilio-inguinal nerve block and wound infiltration for day case herniotomy in children (Reid *et al.*), 658 (f)

Analgesia, postoperative, a comparison of infusions of morphine and ketamine (Owen *et al.*), 1051

Analgesia, postoperative, epidural buprenorphine for (Kumar: Wolff, Carl & Crawford), 79 (c)

Analgesia, postoperative, epidural sufentanil versus intramuscular buprenorphine for (Donadoni & Rolly), 1171

Analgesia, postoperative, for neonates: editorial (Booker), 343

Analgesia and side effects after a single bolus dose during elective Caesarean section; comparison of epidural fentanyl with sufentanil (Madej & Strunin), 1156

Analysers, oxygen, evaluation of (Hunsley: Roe, Tyler & Barnes), 1127 (c)

Anaphylactoid reaction to alcuronium (Pusey *et al.*), 164

Anaphylactoid reaction, cardiac output during (Alston & Oates), 892 (c)

Anaphylactoid reactions to prilocaine (Ruiz *et al.*), 1078

Aneurysm, aortic, surgery, intrathecal morphine in (Davis), 491

Angioneurotic oedema following etomidate/lignocaine (Bricker & Raitt), 323 (c)

Antacid therapy for emergency Caesarean section (Thorburn & Moir), 352

Antibiotic prolongation of neuromuscular blocking effect of vecuronium (Jedeikin *et al.*), 858

Anticholinergic agents, pre-operative, and modification of bradycardia during intra-abdominal surgery (Coventry, McMenemin & Lawrie), 835

Anticoagulant, lupus, implications for obstetric anaesthetists (Malinow *et al.*), 1291

Antiemetic studies with traditional Chinese acupuncture; comparison of manual needling with electrical stimulation and commonly used antiemetics (Ghaly, Fitzpatrick & Dundee), 1108 (f)

Antiemetics, intra-operative, and vomiting after ophthalmic surgery (van den Berg *et al.*), 270

Antipollution device for use with the Jackson–Rees modification of Ayre's T-piece (Paul), 439 (c)

Antipollution device, improved, for the Jackson–Rees modification of the Ayre's T-piece (Spargo, Apadoo & Wilton), 1240 (c)

Anxiety, depression and chronic pain (Jack *et al.*), 1235 (c)

Aortic aneurysm surgery, intrathecal morphine in (Davis), 491

Aortic incompetence, cardiovascular collapse following epidural anaesthesia for Caesarean section in a patient with (Alderson), 643

Aortocoronary bypass graft surgery, comparison of conventional intermittent positive pressure ventilation with high frequency jet ventilation (Normandale *et al.*), 824

APACHE II severity of disease classification system, one year's experience in a general intensive care unit (Jacobs, Chang & Lee), 738

Apnoea, suxamethonium, in a 4-month-old twin (Mehta & Hole), 868

Apples, SI units and Newtons (Rye), 1025 (c)

Argyll tracheal tube, a problem with (Scott & Chapman), 1123 (c)

Arousal from propofol (Hunter, Thornily & Whitburn), 1128 (c)

Arterial cannulation, guide-wire assisted; a complication (McMenemin & Kenny: McGregor), 562 (c)

Arterial to end tidal carbon dioxide tension differences (Fletcher: Shanker *et al.*), 210 (c)

Arterial to end tidal carbon dioxide tension difference during anaesthesia for tubal ligation (Shankar *et al.*), 482

Arterial to end tidal carbon dioxide tension difference during anaesthesia for tubal ligation (Puri: Shankar *et al.*), 1338 (c)

Arterial to end tidal carbon dioxide difference and high frequency jet ventilation (Shankar), 1124 (c)

Arterial oxygen desaturation during postoperative transportation, the influence of operation site (Meiklejohn *et al.*), 1313 (f)

Arterial oxygen saturation during general anaesthesia for paediatric dental extractions (Bone, Galler & Flynn), 879 (f)

Artery, radial, abscess following cannulation of (Lindsay, Kerridge & Collett), 654

Arthroscopy, outpatient, recovery from propofol infusion as the main agent for; comparison with isoflurane (Zuurmond, van Leeuwen & Helmers), 356

Aspiration, pleural, with a central venous catheter (Cooper), 217 (c)

Aspiration, pleural, with a central venous catheter (Thorp), 896 (c)

Association of Anaesthetists' Appeal for the Furnishing and Refurbishment of Nine Bedford Square, London, 105

Association of Anaesthetists of Great Britain and Ireland, 105

Association of Anaesthetists of Great Britain and Ireland, Annual Report of Council 1985–1986, 119

Association of Anaesthetists of Great Britain and Ireland, Junior Anaesthetists' Group, 110

Association of Anaesthetists of Great Britain and Ireland, Linkmen Annual Conference 1986, 459

Asthma, acute, severe, and the menstrual cycle (Lenoir), 1287

Asthma, all that wheezes is not; yet again (Fletcher), 441 (c)

Atelectasis in the lateral decubitus position (Baraka, Moghrabi & Yazigi), 171

Atenolol, prolonged bradycardia and hypotension after neostigmine administration in a patient receiving (Eldor, Hoffman & Davidson), 1294

Atracurium infusion, closed-loop, computer controlled, for steady-state neuromuscular blockade during surgery (Webster & Cohen), 1085
Atracurium infusion, a simple system, feedback control of neuromuscular blockade (Wait, Goat & Blogg), 1212
Atriobronchial fistula, an unusual complication of intravenous feeding in the presence of a mediastinal abscess (Graziotti), 669 (c)
Atropine, tracheal versus intravenous, comparison of the effects on heart rate (Bray, Jones & Grundy), 1188
Audiovisual reviews
  Anaesthesia for children, 98
  Ankle blocks, 96
  Blocks for common paediatric operations, 95
  Burns—nerve blocks of the thigh, 97
  Central venous pressure measurement, 95
  Lower limb nerve blocks, 96
  Lumbar sympathetic block, 97
  Nerve blocks around the knee, 95
Auditory information retention during anaesthesia; study of children who received light general anaesthesia (Standen, Hain & Hosker), 604
Auto-antagonism of buprenorphine (Reynolds), 1334 (c)
Awareness under anaesthesia due to a defective gas-loaded regulator (Puri *et al.*), 539
Axillary block, improving the success rate of (Martin & Dumais), 1117 (c)
Axillary brachial plexus block, quality of, comparison of success rate using perivascular and nerve stimulator techniques (Tuominen *et al.*), 20
Axillary brachial plexus block, quality of (McNicol: Tuominen & Rosenberg), 775 (c)
Axillary vein, a new percutaneous infraclavicular approach to (Nickalls), 151
Ayre's T-piece, an antipollution device for use with the Jackson–Rees modification of (Paul), 439 (c)
Ayre's T-piece, improved antipollution device for the Jackson–Rees modification of (Spargo, Apadoo & Wilton), 1240 (c)

Bain anaesthetic system, gender and obesity index (Shankar *et al.*), 779 (c)
Balloon, blocked, beating the (Cottingham), 673 (c)
Basophil histamine release; a study in allergy to suxamethonium (Withington *et al.*), 850
Benzodiazepines: editorial (Whitwam), 1255
Benzodiazepines, effect on evoked potentials (Milligan, Howard & Dundee: Sebel), 1237 (c)
Benzodiazepines, effects on laryngeal reflexes; comparison of lormetazepam and Diazemuls (Groves, Rees & Rosen), 808
Benzodiazepines and prolonged respiratory depression (Sekar & Mimpriss), 567 (c)
Beta blockade and nitroprusside (Coad: Simpson), 1022 (c)
Beta blockade, suxamethonium and potassium (Goldhill & Martyn), 670 (c)
Beta-blocker treated hypertensive patients, intranasal nitroglycerine attenuates pressor response to tracheal intubation in (Grover *et al.*), 884 (f)
Beta-adrenoreceptor blockade and induced hypotension (Simpson *et al.*), 243
Beta-adrenoceptor blockade and suxamethonium-induced rise in plasma potassium (Maryniak *et al.*), 71 (f)
Betel nut chewing (Divekar), 900 (c)
Blood tests before elective surgery (Jacobsen, Bach & Dalsgaard), 78 (c)
Blood transfusion, survival without, for Jehovah's Witness with severe acute anaemia (Howell & Bamber), 44
Blood warmers, water bath, risk of infection from (Bray), 778 (c)
Book reviews
  ADAMS, HEWITT & ROGERS (EDS): *Emergency anaesthesia*, 787
  ALBRIGHT, FERGUSON II, JOYCE & STEVENSON: *Anaesthesia in obstetrics. Maternal, fetal and neonatal aspects*, 2nd edn, 447
  ALTURA & HALEVY (EDS): *Cardiovascular actions of anesthetics and drugs used in anesthesia. 2. Regional blood flow and clinical considerations*, 1027
  ASTRUP & SEVERINGHAUS (EDS): *The history of blood gases, acids and bases*, 93
  AVELING & INGRAM: *Pastest Part I FFARCS practice exams*, 445
  BEINART: *A history of the Nuffield Department of Anaesthetics, Oxford. 1937–1987*, 1244
  CAMPKIN & TURNER: *Neurosurgical anaesthesia and intensive care*, 2nd edn, 1133
  CARRON, KORBON & ROWLINGSON: *Regional anaesthesia. Techniques and clinical applications*, 333
  CORKE & JACKSON: *Companion to the FFARCS Part III*, 1135
  COVINO & SCOTT: *Handbook of epidural anaesthesia and analgesia*, 330
  DATTA & OSTHEIMER (EDS): *Common problems in obstetric anesthesia*, 1244
  ELLIS & CAMPBELL: *Essential anaesthesia*, 91
  FARBER (ED): *Infection control in intensive care*, 1245
  FELTS (ED): *Clinics in anaesthesiology, Vol. 4 No. 4. Anesthesia and the geriatric patient*, 1028
  Health equipment information No. 155: Evaluation of ECG recorders, 94
  Health equipment information No. 157: Evaluation of infusion pumps and controllers, 94

HINDS: *Intensive care. A concise textbook*, 1133
JONES, BERGMANN, LASSNER, OTTENI & THOMSON (EDS): *Current European anaesthesiology*, 1130
KAUFMAN (ED): *Anaesthesia review 4*, 1132
KHARKEVICH (ED): *New neuromuscular blocking agents. Handbook of experimental pharmacology*, 332
KING (ED): *Primary anaesthesia*, 333
LUNN: *Lecture notes on anaesthetics*, 3rd edn, 446
LUNN (ED): *Epidemiology in anaesthesia*, 332
MILLER (ED): *Anesthesia*, 92
MILLER, KIRBY, OSTHEIMER, SAIDMAN & STOELTING (EDS): *1986 yearbook of anesthesia*, 1134
MOIR & THORBURN: *Obstetric anaesthesia and analgesia*, 3rd edn, 446
MORGAN (ED): *Problems in obstetric anaesthesia*, 788
MISHIN & JONES: *Physics for the anaesthetist*, 4th edn, 1130
NOVELLI & URSINI (EDS): *Oxygen free radicals in shock*, 445
NUWER: *Evoked potential monitoring in the operating room*, 786
OSTHEIMER (ED): *Clinics in anaesthesiology. Obstetric analgesia and anaesthesia I and II*, 91
PAGE, MILLS & MORTON: *A colour atlas of cardio-pulmonary resuscitation techniques*, 448
PHILLIPS & ODGERS: *Parenteral and enteral nutrition*, 92
RAJ (ED): *Practical management of pain*, 1132
RIPPE, IRWIN, ALPERT & DALEN (EDS): *Intensive care medicine*, 331
SHOEMAKER & ABRAHAM (EDS): *Diagnostic methods in critical care. Automated data collection and interpretation*, 1131
SCHNIDER & LEVINSON (EDS): *Anesthesia for obstetrics*, 2nd edn, 786
SIMPSON & GOODMAN: *600 MCQs in anaesthesia: clinical practice*, 1027
SNYDER & PINSKY (EDS): *Oxygen transport in the critically ill*, 1026
STANLEY & PETTY (EDS): *Anesthesiology 1986*, 92
STEPHEN & ASSAF (EDS): *Geriatric anaesthesia. Principles and practice*, 1026
STEVENS (ED): *Clinics in anaesthesiology. Preparation for anaesthesia*, 90
STOELTING, BARASH & GALLAGHER (EDS): *Advances in anesthesia, Vol. 4*, 1134
TAYLOR (ED): *Cardiopulmonary bypass*, 331
Bowel sounds (Payne-James, Rees & Silk), 893 (c)
Bowel sounds during artificial ventilation (Manara, Kinnear & Park), 668 (c)
Bowel sounds during intermittent positive pressure ventilation (Shelly & Church), 207 (c)
Brachial plexus block, unilateral thoraco-abdominal blockade following the supraclavicular approach (Manara), 757
Bradycardia associated with the use of vecuronium, a comparative study with pancuronium with and without glycopyrronium (Cozanitis, Pouttu & Rosenberg), 192 (f)
Bradycardia during elevation of zygomatic fractures, a variation of the oculocardiac reflex (Shearer & Wenstone), 1207
Bradycardia during intra-abdominal surgery, modification by pre-operative anticholinergic agents (Coventry, McMenemin & Lawrie), 835
Bradycardia after propofol infusion (Thomson & Yate), 430 (c)
Bradycardia, prolonged, and hypotension after neostigmine administration in a patient receiving atenolol (Eldor, Hoffman & Davidson), 1294
Bradycardia and hypotension in spinal anaesthesia (Hutter), 89 (c)
Breathing systems, circle absorption, nomenclature of (Horsey: Twigley, Chakrabarti & Whitwam), 1018 (c)
Breathing systems, closed, a new ventilator for (Twigley, Chakrabarti & Whitwam), 419
Breathing systems, closed, a new ventilator for (James: Plenderleith: Twigley, Chakrabarti & Whitwam), 1335 (c)
Breathing systems, minimum fresh gas flow requirements of, during spontaneous ventilation; a graphical approach (Dorrington & Lehane), 732
Breathing systems, multipurpose (Humphrey: Calhaem), 88 (c)
Breathing systems, a test for (Cooper), 1019 (c)
Bronchial intubation, difficult (Russell, Frazer & Richardson), 82 (c)
Bronchial intubation, difficult (Skinner), 567 (c)
Bronchial intubation, selective (Welsh), 82 (c)
Bronchial stents, use in the management of bronchomalacia (Goddard & Booker), 534
Bronchial tubes, correct placement of (MacGillivray, Rocke & Mahomedy), 570 (c)
Bronchomalacia, use of bronchial stents in the management of (Goddard & Booker), 534
Bronchoscopic mask, Brünings' (Condon), 996
Bronchoscopy, carbon dioxide laser, a review of problems and complications (Conacher, Paes & Morritt), 511
Bronchospasm and ergometrine (Hill *et al.*), 1115 (c)
Bronchospasm, kinked tube or? (Ross), 441 (c)
Brünings' bronchoscopic mask (Condon), 996
Budd–Chiari syndrome, peri-operative management of a patient with; paroxysmal nocturnal haemoglobinuria (Taylor, Whitwam & Worsley), 639
Bullectomy, bilateral, high frequency jet ventilation for (McCarthy *et al.*), 411

Bupivacaine, hyperbaric, compared with hyperbaric lignocaine for subarachnoid block (Ewart & Rubin), 1183
Bupivacaine, spread in the epidural space, and speed of injection (Griffiths *et al.*), 160
Buprenorphine auto-antagonism (Reynolds), 1334 (c)
Buprenorphine, epidural, for postoperative analgesia (Kumar: Wolff, Carl & Crawford), 79 (c)
Buprenorphine, epidural, prolonged and biphasic respiratory depression following (Jensen *et al.*), 470
Buprenorphine, intramuscular, versus epidural sufentanil for postoperative analgesia (Donadoni & Rolly), 1171
Buprenorphine and prolonged respiratory depression (Sekar & Mimpriss), 567 (c)

Caesarean section, cardiovascular collapse following epidural anaesthesia for, in a patient with aortic incompetence (Alderson), 643
Caesarean section, cardiovascular collapse following epidural anaesthesia for (Brighouse: Grebenik, Orlikowski & Barber: Mitchell & Downing: MacKenzie: Crawford: Alderson), 1226 (c)
Caesarean section, elective, analgesia and side effects after a single bolus dose of epidural fentanyl or sufentanil during (Madej & Strunin), 1156
Caesarean section, elective, epidural anaesthesia for (Laishley, Reynolds & Morgan: Crawford), 554 (c)
Caesarean section, elective, epidural block for (Severn: Crawford), 435 (c)
Caesarean section, emergency, antacid therapy for (Thorburn & Moir), 352
Caesarean section, epidural block for (Shah: Crawford), 327 (c)
Caesarean section, spinal anaesthesia for (Hollis, White & Procter), 323 (c)
Caesarean section, spinal anaesthesia (Kirkwood), 900 (c)
Caesarean section, urgent, anaesthetic management; unstable cervical fracture (Eason *et al.*), 745
Cancer, advanced, a double-blind trial of controlled release morphine tablets in patients with (Hanks, Twycross & Bliss), 840
Cancer patient, spinal cord compression during chronic epidural morphine administration in (van Diejen, Driessen & Kaanders), 1201
Cannulae, intravenous, flow through (Kestin), 67
Cannulation, arterial, guide-wire assisted; a complication (McMenemin & Kenny: McGregor), 562 (c)
Cannulation of the radial artery, abscess following (Lindsay, Kerridge & Collett), 654
Cannulation, radial artery, local tissue oxygenation after (Murray & Mowbray), 1070
Capnograph, leak detection with (Martin), 1025 (c)
Capnography (Cooper), 1238 (c)
Carbon dioxide, arterial to end tidal tension differences (Fletcher: Shankar *et al.*), 210 (c)
Carbon dioxide, arterial to end tidal tension difference during anaesthesia for tubal ligation (Shankar *et al.*), 482
Carbon dioxide, arterial to end tidal tension difference during anaesthesia for tubal ligation (Puri: Shankar *et al.*), 1338 (c)
Carbon dioxide, arterial to end tidal difference and high frequency jet ventilation (Shankar), 1124 (c)
Carbon dioxide laser bronchoscopy, a review of problems and complications (Conacher, Paes & Morritt), 511
Carbon dioxide laser surgery in tracheobronchial lesions, anaesthetic management (Hunton & Oswal), 1222 (f)
Carbon dioxide, sampling for (Allen & Wren), 560 (c)
Carcinoid syndrome, anaesthesia, and somatostatin; peri-operative administration of a somatostatin analogue to suppress carcinoid tumour activity (Roy, Carter & Wright), 627
Carcinoid syndrome and intravenous cyproheptadine (Solares *et al.*), 989
Cardiac anaesthesia, memory of; psychological sequelae in cardiac patients of intra-operative suggestion and operating room conversation (Goldman, Shah & Hebden), 596
Cardiac arrest in near-term pregnancy (Lindsay & Hanson), 1074
Cardiac arrests, a basic problem at (Dumont & Mousdale), 1018 (c)
Cardiac dysrhythmias, in the dental chair, incidence during anaesthesia with halothane and isoflurane (Cripps & Edmondson), 189 (f)
Cardiac dysrythmias during oral surgery, influence of premedication on the occurrence of (Smith & O'Connell), 882 (f)
Cardiac dysrhythmia after subtrigonal phenol (Forrest & Ramage), 777 (c)
Cardiac output during an anaphylactoid reaction (Alston & Oates), 892 (c)
Cardiac surgery, acute effects of intravenous isosorbide dinitrate during (Parsons, Wetzel & Mohandas), 498
Cardiac surgery, continuous display of plasma potassium during (Drake, Treasure & Smith), 23
Cardiac surgery, fixed dilated pupils following (Carter & Weston), 1231 (c)
Cardiac valvular surgery, comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation (Sherry, Windsor & Feneck), 1276
Cardioplegia, resistance to (Miller & Dougall), 1117 (c)
Cardiopulmonary bypass, insertion of intratracheal stents (Sherry *et al.*), 61
Cardiopulmonary resuscitation in district general hospitals (Newman), 314 (c)
Cardiovascular collapse following epidural anaesthesia for Caesarean section in a patient with aortic incompetence (Alderson), 643
Cardiovascular collapse following epidural anaesthesia for Caesarean section (Brighouse: Grebenik, Orlikowski & Barber: Mitchell & Downing: MacKenzie: Crawford: Alderson), 1226 (c)

Cardiovascular function compared, in one lung anaesthesia, during conventional ventilation and high frequency jet ventilation (Jenkins *et al.*), 938
Cardiovascular responses during splenectomy and splenorenal shunt formation in a patient with systemic mastocytosis (Smith *et al.*), 861
Cardiovascular responses to tracheal intubation, the effect of sufentanil on (Kay *et al.*), 382
Carminative property of peppermint in magnesium trisilicate mixture, BP (Robson), 776 (c)
Carotid artery surgery, cervical epidural analgesia during (Campkin: Kainuma & Shimada), 437 (c)
Carotid sinus massage, pre-operative, value of (McConachie), 636
Cataract surgery, intravenous sedation (Gilbert *et al.*), 1063
Catheter, central venous, pleural aspiration with (Cooper), 217 (c)
Catheter, central venous, pleural aspiration with (Thorp), 896 (c)
Catheters, epidural, fixation of (Mason, Edmondson & McHugh), 672 (c)
Catheters, epidural, long-term, failure of (Brasseur *et al.*), 557 (c)
Catheter, epidural, migration during labour (Phillips & Macdonald), 661 (f)
Catheters, epidural, severance of (Hutchison), 182
Catheters, epidural, severance of (Butchers: Hutchison), 315 (c)
Catheterisation, intercostal, an alternative approach to the paravertebral space (Mowbray, Wong & Murray), 958
Catheterisation, pulmonary artery, benefits of (Wilkins & Edwards: Stoddart), 436 (c)
Catheterisation, subdural, accidental (Treffers & de Lange: Lee & Dodd), 556 (c)
Caudal epidurals—a further caution (Shah), 440 (c)
Caudal epidural—possible subdural spread? (Reynolds), 440 (c)
Cellulitis as a complication of difficult tracheal intubation (Young & Robinson), 569 (c)
Central venous catheter, pleural aspiration with (Cooper), 217 (c)
Central venous catheter, pleural aspiration with (Thorp), 896 (c)
Central venous pressure, spurious (Barrowcliffe), 293
Cerebral tumour, epidural anaesthesia in the presence of (Chater, Greig & Sugden: Kinsella: Francis: Goroszeniuk & Wright), 433 (c)
Cervical epidural analgesia during carotid artery surgery (Campkin: Kainuma & Shimada), 437 (c)
Cervical epidural anaesthesia; if nothing goes wrong—is everything alright? (Sold & Weis: Kainuma & Shimada), 557 (c)
Cervical fracture, unstable; anaesthetic management for an urgent Caesarean section (Eason *et al.*), 745
Cervical fracture, unstable (Braude: Eason, Swaine & Jones), 1334 (c)
Chewing of betel nuts (Divekar), 900 (c)
Chewing gum, to chew or not to chew (Cohen), 220 (c)
Children, day case herniotomy; comparison of ilio-inguinal nerve block and wound infiltration for postoperative analgesia (Reid *et al.*), 685 (f)
Children, electromyographic studies; liver tumours and muscle relaxants (Brown *et al.*), 1284
Children and explosive anaesthetics (Lett), 443 (c)
Children and explosive anaesthetics (Williams), 212 (c)
Children, intercostal nerve blockade (Shelly & Park), 541 (f)
Children, who received light general anaesthesia; retention of auditory information presented during anaesthesia (Standen, Hain & Hosker), 604
Children, lorazepam in a fast dissolving dose form as a premedicant for (Underhill, Bush & Harper), 319 (c)
Children, peak intratracheal pressure during controlled ventilation in; computer study of the Servo 900C ventilator (Synnott, Wren & Davenport), 719
Children, comparison of two regional techniques for postoperative analgesia following herniotomy and orchidopexy (Cross & Barrett), 845
Children, respiratory depression at different and tidal halothane concentrations (Lindahl, Yates & Hatch), 1267
Children, a simple device for assessment of local anaesthetic blocks in (Cross), 84 (c)
Children, spontaneously breathing, respiratory effects of halothane, enflurane and halothane in (Murat *et al.*), 711
Children, young, anaesthesia and intra-ocular pressure in; a study of three different techniques of anaesthesia (Dear *et al.*), 259
Circle system, expiratory obstruction in (Alston), 1120 (c)
Classification system, APACHE II, severity of disease; one year's experience in a general intensive care unit (Jacobs, Chang & Lee), 738
Clinical investigations—why we must keep control: editorial (Aitkenhead), 583
Clinitron bed, treatment of severe accidental hypothermia using (Miles & Thompson), 415
Clinitron bed, treatment of accidental hypothermia with (Lloyd: Miles & Thompson), 1121 (c)
Closed-loop administration of atracurium; steady-state neuromuscular blockade during surgery using a computer controlled closed-loop atracurium infusion (Webster & Cohen), 1085
Clutton-Brock, Professor John (Baskett), 426 (c)
Coaxial tube, inner, unattached (Roberts), 1128 (c)
Cold injury and hyperkalaemia (Martyn & Goldhill), 561 (c)
Committee on Safety of Medicines, and halothane (Vance), 212 (c)
Complications of difficult intubation (Mostafa), 1241 (c)

Complication on induction of anaesthesia: respiratory obstruction following vocal cord injection (Bodenham, Latimer & Bethune), 289

Complications, postoperative, of dystrophia myotonica (Aldridge), 1121 (c)

Complications, postoperative, of dystrophia myotonica (Moore & Moore), 529

Complications, postoperative, of dystrophia myotonica (Zuck: Moore & Moore), 1023 (c)

Complications and problems of carbon dioxide laser bronchoscopy; a review (Conacher, Paes & Morritt), 511

Complication, unusual, of intravenous feeding in the presence of mediastinal abscess; atriobronchial fistula (Graziotti), 669 (c)

Computer controlled closed-loop atracurium infusion, steady state neuromuscular blockade during surgery using (Webster & Cohen), 1085

Computer program index, 449, 902

Concurrent drug therapy in patients undergoing surgery (Duthie *et al.*), 305 (f)

Consent for epidural analgesia (Sneyd), 1232 (c)

Contaminated Marcain ampoule (Sugden & Bembridge: Watson), 87 (c)

Contamination of ampoules (Kirkpatrick), 779 (c)

Contamination control in long-term ventilation, a clinical study using a heat- and moisture-exchanging filter (Gallagher, Strangeways & Allt-Graham), 476

Continuous airway pressure, safety of a new system for (Clayton & Catling), 440 (c)

Continuous infusion epidural analgesia, loading dose for; technique to reduce the incidence of hypotension (MacLeod *et al.*), 377

Continuous positive airway pressure, and total collapse of lung (Davies & Grant), 780 (c)

Controlled release morphine tablets, a double-blind trial in patients with advanced cancer (Hanks, Twycross & Bliss), 840

Convulsions, delayed, after day case anaesthesia with enflurane (Fahy), 1327 (c)

Coronary artery bypass surgery in a patient with suspected malignant hyperpyrexia, propofol infusion for (Richardson), 1125 (c)

Courses in anaesthesia, 1037, 1151

CPAP *see* Continuous positive airway pressure

Creatine kinase, effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on (Laurence), 503

Cricoid yoke (Brain: Howells), 780 (c)

Critically ill patient, use of ketamine infusion as a sedative, inotrope and bronchodilator (Part *et al.*), 980

Croup, nebulised adrenaline and preservatives (Hinton & Goss), 436 (c)

Cyclopropane (Lamberty), 212 (c)

Cyclopropane, a regional survey on the use of (Konarzewski *et al.*), 186 (f)

Cylinder yokes, empty, potential leaks through (McQuillan & Jackson), 1308

Cyproheptadine, intravenous, and carcinoid syndrome (Solares *et al.*), 989

Cysts, epiglottic, asymptomatic, as a cause of upper airway obstruction during anaesthesia (Mason & Wark), 407

Cyst, ovarian, giant, removal of; anaesthetic and intensive care management (Morrison & Morgan), 965

Day case anaesthesia with enflurane, delayed convulsions after (Fahy), 1327 (c)

Day case anaesthesia, oculogyric crisis after (Dingwall), 565 (c)

Day case herniotomy in children, comparison of ilio-inguinal nerve block and wound infiltration for postoperative analgesia (Reid *et al.*), 685 (f)

Day case isoflurane anaesthesia, comparison of propofol and methohexitone as induction agents (O'Toole *et al.*), 373

Day case surgery premedication, a study of oral midazolam (Raybould & Bradshaw), 591

Day case termination of pregnancy, nausea and vomiting after prostaglandins in; efficacy of low dose droperidol (Millar & Hall), 613

Death following two enflurane anaesthetics (Paull & Fortune), 1191

Delivery and labour, management in a patient with Guillain–Barré syndrome (McGrady), 899 (c)

Dental chair, anaesthesia in; comparison of the incidence of cardiac dysrhythmias during anaesthesia with halothane and isoflurane (Cripps & Edmondson), 189 (f)

Dental extractions, paediatric, arterial oxygen saturation during general anaesthesia for (Bone, Galler & Flynn), 879 (f)

Depression, anxiety and chronic pain (Jack *et al.*), 1235 (c)

Diamorphine in aqueous solution (Macrae), 82 (c)

Diamorphine stability and pharmacodynamics (Hanks, Hoskin & Walker), 664 (c)

Diazemuls and lormetazepam, comparison of their effects on laryngeal reflexes (Groves, Rees & Rosen), 808

Diazepam, evoked potentials following (Loughnan *et al.*), 195 (f)

Diclofenac sodium, morphine sparing effects of, following abdominal surgery (Hodsman *et al.*), 1005 (f)

Difficult circumstances, anaesthesia in (Wilson & Sinclair), 443 (c)

Difficult extubation, *see* Extubation

Difficult intubation, *see* Intubation

Diluted drugs, manufactured for paediatric anaesthesia (Laishley), 213 (c)

Disconnexion hazard (Goldberg), 219 (c)
Disseminated intravascular coagulation, fatal, following a monoamine oxidase inhibitor/tricyclic interaction (Tackley & Tregaskis), 760
District general hospitals, cardiopulmonary resuscitation in (Newman), 314 (c)
Dopamine, low dose infusion (Salem), 572 (c)
Dopamine, lose dose, the prevention of renal impairment in patients undergoing orthotopic liver grafting by infusion of (Polson *et al.*), 15
Dose *see* Test dose
Drawover air anaesthesia with the Triservice anaesthetic apparatus; halothane and trichloroethylene compared with isoflurane (Tighe & Pethybridge), 887 (f)
Drawover anaesthesia system, isoflurane in (Yoganathan & Houghton), 1241 (c)
Drawover anaesthetic systems, factors determining the inspired oxygen concentration (Mackie), 299
Drawover system, reservoir volume in (Yoganathan, Johnston & Houghton: Mackie), 1337 (c)
Droperidol with fentanyl, fentanyl, and halothane anaesthesia, a comparison of their effects on intra-ocular pressure in adults (Feneck & Durkin), 266
Droperidol, low dose, efficacy; nausea and vomiting after prostaglandins in day case termination of pregnancy (Millar & Hall), 613
Drug dilutions, manufactured, for paediatric anaesthesia (Laishley), 213 (c)
Drug therapy, concurrent, in patients undergoing surgery (Duthie *et al.*), 305 (f)
Dural puncture, unintentional, a survey of recognition and management (Okell & Sprigge), 1110 (f)
Dystrophia myotonica, postoperative complications of (Aldridge), 1121 (c)
Dystrophia myotonica, postoperative complications of (Moore & Moore), 529
Dystrophia myotonica, postoperative complications of (Zuck: Moore & Moore), 1023 (c)

Ear, middle, surgery, hypotensive anaesthesia for (Williamson; Eltringham & Fairbairn), 669 (c)
Editorials
  Benzodiazepines (Whitwam), 1255
  Bursting the alveolar bubble (Hills), 467
  Clinical investigations—why we must keep control (Aitkenhead), 583
  Down the tube (Greenbaum), 927
  Future organisation of anaesthetic health care (Rosen), 1043
  Minimal monitoring and vigilance (Mathias & Lunn), 683
  Postoperative analgesia for neonates? (Booker), 343
  Sir Ivan Whiteside Magill (Edridge), 231
  Smoking and anaesthesia (Jones, Rosen & Seymour), 1
  The EEG and awareness during anaesthesia (Mori), 1153
  The health of anaesthetists (Harrington), 131
  Zidovudine and the anaesthetist (Phillips & Spence), 799
EEG and awareness during anaesthesia: editorial (Mori), 1153
Elderly, morphine-induced respiratory depression in the (Bourke: Bowen *et al.*), 428 (c)
Electroconvulsive therapy, oxygenation during (Wood: Sneyd: Hanning, Lew & Eastley), 431 (c)
Electroconvulsive therapy, oxygenation during (Simpson, Chater & Swindells: Hanning, Lew & Eastley), 1234 (c)
Electromyographic studies in children; liver tumours and muscle relaxants (Brown *et al.*), 1284
Emergency eye surgery, control of intra-ocular pressure during the induction of anaesthesia; a high dose vecuronium technique (Abbott & Samuel), 1008 (f)
Encephalopathy, hypoglycaemic, following surgery on phaeochromocytoma (Channa *et al.*), 1298
End tidal to arterial carbon dioxide tension differences (Fletcher: Shankar *et al.*), 210 (c)
End tidal to arterial carbon dioxide tension difference during anaesthesia for tubal ligation (Shankar *et al.*), 482
End tidal to arterial carbon dioxide tension difference during anaesthesia for tubal ligation (Puri: Shankar *et al.*), 1338 (c)
End tidal to arterial carbon dioxide difference and high frequency jet ventilation (Shankar), 1124 (c)
End tidal halothane concentrations, and respiratory depression in children (Lindahl, Yates & Hatch), 1267
Enflurane anaesthetics, two, hepatotoxicity and death following (Paull & Fortune), 1191
Enflurane, delayed convulsions after day case anaesthesia with (Fahy), 1327 (c)
Enflurane and isoflurane as alternatives to halothane; Triservice anaesthetic apparatus (Kocan), 1101 (f)
Enflurane compared with isoflurane anaesthesia; serum fluoride levels in morbidly obese patients (Strube, Hulands & Halsey), 685
Enflurane, respiratory effects in spontaneously breathing children (Murat *et al.*), 711
Enflurane and trichloroethylene compared as adjuncts to nitrous oxide and relaxant anaesthesia (Rich & Reynolds), 1320 (f)
Epidural anaesthesia for Caesarean section in a patient with aortic incompetence, cardiovascular collapse following (Alderson), 643
Epidural anaesthesia for Caesarean section, cardiovascular collapse following (Brighouse: Grebenik, Orlikowski & Barber: Mitchell & Downing: MacKenzie: Crawford: Alderson), 1226 (c)
Epidural anaesthesia for elective Caesarean section (Laishley, Reynolds & Morgan: Crawford), 554 (c)

Epidural anaesthesia in the presence of a cerebral tumour (Chater, Greig & Sugden: Kinsella: Francis: Goroszeniuk & Wright), 433 (c)
Epidural anaesthesia, cervical; if nothing goes wrong—is everything alright? (Sold & Weis: Kainuma & Shimada), 557 (c)
Epidural analgesia, cervical, during carotid artery surgery (Campkin: Kainuma & Shimada), 437 (c)
Epidural analgesia, consent for (Sneyd), 1232 (c)
Epidural analgesia, continuous infusion, loading dose for; technique to reduce the incidence of hypotension (MacLeod *et al.*), 377
Epidural block for Caesarean section (Shah: Crawford), 327 (c)
Epidural block for elective Caesarean section (Severn: Crawford), 435 (c)
Epidural buprenorphine for postoperative analgesia (Kumar: Wolff, Carl & Crawford), 79 (c)
Epidural buprenorphine, prolonged and biphasic respiratory depression following (Jensen *et al.*), 470
Epidural catheters, fixation of (Mason, Edmondson & McHugh), 672 (c)
Epidural catheters, long-term, failure of (Brasseur *et al.*), 557 (c)
Epidural catheter, migration during labour (Phillips & Macdonald), 661 (f)
Epidural catheters, severance of (Hutchison), 182
Epidural catheters, severance of (Butchers: Hutchison), 315 (c)
Epidural, caudal; possible subdural spread? (Reynolds), 440 (c)
Epidurals, caudal; a further caution (Shah), 440 (c)
Epidural fentanyl, comparison with sufentanil; analgesia and side effects after a single bolus dose during elective Caesarean section (Madej & Strunin), 1156
Epidural hydromorphone, delayed respiratory arrest after (Wüst & Bromage), 404
Epidural infusion technique for labour (Gaylard, Wilson & Balmer), 1098 (f)
Epidural injection, speed of (Lavies), 783 (c)
Epidural lavage for extensive epidural suppuration (Cardan & Nanulescu), 1023 (c)
Epidural meptazinol (Rao *et al.*), 218 (c)
Epidural morphine administration, chronic, in a cancer patient, spinal cord compression during (van Diejen, Driessen & Kaanders), 1201
Epidural needle, *in vitro* study of the effect of rotation of (Meiklejohn), 1180
Epidural, obstetric, test doses (Cartwright), 556 (c)
Epidural opioid long-term therapy; respiratory depression after intrathecal opioids (Krantz & Christensen), 168
Epidural space, identification of (Wait), 1231 (c)
Epidural space, speed of injection and spread of bupivacaine in (Griffiths *et al.*), 160
Epidural sufentanil versus intramuscular buprenorphine for postoperative analgesia (Donadoni & Rolly), 1171
Epidural sufentanil, respiratory arrest after (Blackburn), 665 (c)
Epidural large dose sufentanil; management of postoperative pain with few side effects (Madej, Watson & Martin), 1204
Epiglottic cysts, asymptomatic, as a cause of upper airway obstruction during anaesthesia (Mason & Wark), 407
Equipment leasing (Wauchob), 219 (c)
Equipment, unwanted (Emmanuel & Dye), 220 (c)
Ergometrine and bronchospasm (Hill *et al.*), 1115 (c)
Ether, a regional survey on the use of (Konarzewski *et al.*), 186 (f)
Etomidate anaesthesia for laparoscopy, comparison with propofol, thiopentone and isoflurane (de Grood *et al.*), 815
Etomidate/lignocaine, angioneurotic oedema following (Bricker & Raitt), 323 (c)
Etomidate and propofol compared in microlaryngeal surgery (de Grood *et al.*), 366
Evoked potentials, the effect of benzodiazepines on (Milligan, Howard & Dundee: Sebel), 1237 (c)
Evoked potentials following diazepam or fentanyl (Loughnan *et al.*), 195 (f)
Exchangers, heat and moisture, efficiency of (Turner & Wright: Lowe), 1117 (c)
Exchangers, heat and moisture (Replyuk), 1120 (c)
Expiratory obstruction in a circle system (Alston), 1120 (c)
Expiratory obstruction, complete, an unusual cause of (Jack), 564 (c)
Explosive anaesthetic agents; a regional survey on the use of ether and cyclopropane (Konarzewski *et al.*), 186 (f)
Explosive anaesthetics and children (Williams), 212 (c)
Explosive anaesthetics and children (Lett), 443 (c)
Extracorporeal shock wave lithotripsy (Economacos *et al.*), 779 (c)
Extradural pressures, and hanging drop (McKinney), 1132 (c)
Extubation difficulty (Wood), 220 (c)
Extubation, difficult (Buckley & Bush), 778 (c)
Extubation, difficult, due to a kinked pilot tube (Mehta), 443 (c)
Eye surgery, emergency, control of intra-ocular pressure during the induction of anaesthesia; a high dose vecuronium technique (Abbott & Samuel), 1008 (f)
Eye surgery, prochlorperazine and vomiting after (van den Berg & Lambourne), 898 (c)
Eye *see also* Ophthalmic

Facet joint injection, spinal anaesthesia following; report of two cases (Goldstone & Pennant), 754
Faculty of Anaesthetists of the Royal College of Surgeons of England, 110
Faculty of Anaesthetists of the Royal College of Surgeons in Ireland, 111
Failed tracheal intubation, propofol in (Coleman & Phillips), 1233 (c)
Failure of long-term epidural catheters (Brasseur *et al.*), 557 (c)
Faints, supine (Paul & McKeown), 1120 (c)
Fatal disseminated intravascular coagulation following a monoamine oxidase inhibitor/tricyclic interaction (Tackley & Tregaskis), 760
Feedback control of neuromuscular blockade; a simple system for infusion of atracurium (Wait, Goat & Blogg), 1212
Feedback during patient-controlled analgesia using a speech synthesiser (Hodsman *et al.*), 767 (f)
Fentanyl bolus administration compared with three alfentanil infusion regimens (Stuart-Taylor & Sleigh), 1218 (f)
Fentanyl, droperidol with fentanyl, and halothane anaesthesia, a comparison of their effects on intra-ocular pressure in adults (Feneck & Durkin), 266
Fentanyl, evoked potentials following (Loughnan *et al.*), 195 (f)
Fentanyl and sufentanil, epidural, a comparison; analgesia and side effects after a single bolus dose during elective Caesarean section (Madej & Strunin), 1156
Fibreoptic intubation, transillumination in (Whitlock & Calder), 570 (c)
Fibreoptic techniques, training (Mostafa), 429 (c)
Filter, heat- and moisture-exchanging, use in clinical study of contamination control in long-term ventilation (Gallagher, Strangeways & Allt-Graham), 476
Filters, humidification by (Kent: Allt-Graham, Gallagher & Strangeways), 1119 (c)
Flow through intravenous cannulae (Kestin), 67
Fluids, peri-operative (Bennett: Hillman), 570 (c)
Fluoride, serum levels in morbidly obese patients; enflurane compared with isoflurane anaesthesia (Strube, Hulands & Halsey), 685
Fluorocarbons, current status and future applications (Faithfull), 234
Force, applied, unit of (Wilson), 86 (c)
Forceps, Magill, modified, for difficult tracheal intubation (Pelimon & Simunovic), 83 (c)
Forceps, Magill, modified, for difficult tracheal intubation (Vonwiller, Liberman & Maver), 777 (c)
Fracture, cervical, unstable; anaesthetic management for an urgent Caesarean section (Eason *et al.*), 745
Fracture, cervical, unstable (Braude: Eason, Swaine & Jones), 1334 (c)
Fractures, zygomatic, bradycardia during elevation of; a variation of the oculocardiac reflux (Shearer & Wenstone), 1207

Gas flow requirements of anaesthetic breathing systems during spontaneous ventilation; a graphical approach (Dorrington & Lehane), 732
Gastric emptying and small bowel transit times in volunteers after intravenous morphine and nalbuphine (Yukioka *et al.*), 704
Gelatins, new generation, review of their history, manufacture and properties (Saddler & Horsey), 998
Gender, Bain anaesthetic system and obesity index (Shankar *et al.*), 779 (c)
General anaesthesia, should air–oxygen replace nitrous oxide–oxygen in? (Moseley *et al.*), 609
General anaesthesia, light, in children, and retention of auditory information presented during anaesthesia (Standen, Hain & Hosker), 604
General anaesthesia for paediatric dental extractions, arterial oxygen saturation during (Bone, Galler & Flynn), 879 (f)
Glucose 6-phosphate dehydrogenase deficiency and anaesthesia, a case report and review of the literature (Smith & Snowdon), 281
Glycine, a red patient with immunological reaction to? (Moskovits, Riches & Soni), 692
Glycopyrronium, a comparative study of bradycardia associated with vecuronium and pancuronium, with and without (Cozanitis, Pouttu & Rosenberg), 192 (f)
Graseby PCAS pumps—a potential hazard (Hanning, Ogden & Parry: Coombes), 559 (c)
Grass FT03 transducer, limitations of (Sosis: Jones), 85 (c)
Guanethidine intravenous block, a case of prolonged hypotension following (Sharpe, Milaszkiewicz & Carli), 1081
Guide wire, *see* Wire
Guillain–Barré syndrome, management of labour and delivery in a patient with (McGrady), 899 (c)

Haemodynamic disturbance, prolonged, following attempted retrobulbar block (Cardan, Pop & Negrutiu), 668 (c)
Haemodynamic effects, comparison of intermittent positive pressure ventilation with high frequency jet ventilation following valvular heart surgery (Sherry, Windsor & Feneck), 1276
Haemoglobinuria, nocturnal, paroxysmal; peri-operative management of a patient with Budd–Chiari syndrome (Taylor, Whitwam & Worsley), 639
Haemonetic cell saver (Lindop *et al.*), 85 (c)
Haemorrhage, retrobulbar, spontaneous, following anaesthesia (Gunning & Collett), 875
Hallucinations after anaesthesia (Lloyd), 1015 (c)

Halothane and the Committee on Safety of Medicines (Vance), 212 (c)
Halothane end tidal concentrations, and respiratory depression in children (Lindahl, Yates & Hatch), 1267
Halothane, fentanyl, and droperidol with fentanyl, a comparison of their effects on intra-ocular pressure in adults (Feneck & Durkin), 266
Halothane and isoflurane anaesthesia in the dental chair, a comparison of the incidence of cardiac dysrhythmias (Cripps & Edmondson), 189 (f)
Halothane, repeated use of (Macmillan & Colville), 1017 (c)
Halothane, respiratory effects in spontaneously breathing children (Murat *et al.*), 711
Halothane specific antibody (Williams), 444 (c)
Halothane, trial of isoflurane and enflurane as alternatives to; Triservice anaesthetic apparatus (Kocan), 1101 (f)
Halothane and trichloroethylene compared with isoflurane, a study of drawover air anaesthesia with the Triservice anaesthetic apparatus (Tighe & Pethybridge), 887 (f)
Halothane, unexplained hepatitis following (Burns), 76 (c)
Hanging drop and extradural pressures (McKinney), 1132 (c)
Hazard on anaesthetic machines (Bamber), 782 (c)
Hazard, disconnexion (Goldberg), 219 (c)
Hazard of free-standing vaporizers (Van Besouw & Thurlow), 671 (c)
Hazard Notice, 797, 925
Hazard with the Penlon off-line vaporizer mounting system (Woollam), 781 (c)
Hazard, potential, of Graseby PCAS pumps (Hanning, Ogden & Parry: Coombs), 559 (c)
Hazard of silencers for jet ventilators (Van Besouw), 81 (c)
Headache, postoperative, in young patients after spinal anaesthesia (Flaatten *et al.*), 202 (f)
Health of anaesthetists: editorial (Harrington), 131
Hearing loss and nitrous oxide (Coe), 1230 (c)
Hearing loss, transient, following spinal anaesthesia (Wang, Fog & Bove), 1258
Heart and lung transplantation, combined, anaesthesia for (Sale *et al.*), 249
Heart rate, comparison of the effects of tracheal and intravenous atropine on (Bray, Jones & Grundy), 1188
Heat and moisture exchangers (Replyuk), 1120 (c)
Heat and moisture exchangers, efficiency of (Turner & Wright: Lowe), 1117 (c)
Heat- and moisture-exchanging filter, use in clinical study of contamination control in long-term ventilation (Gallagher, Strangeways & Allt-Graham), 476
Hepatitis, unexplained, following halothane (Burns), 76 (c)
Hepatitis B, serological markers for (Newcombe), 1239 (c)
Hepatitis B virus infection, the prevalence of serological markers for, amongst anaesthetists in the Oxford region (Sinclair, Ashby & Kurtz), 30
Hepatotoxicity and death following two enflurane anaesthetics (Paull & Fortune), 1191
Herniotomy, day case, in children; comparison of ilio-inguinal nerve block and wound infiltration for postoperative analgesia (Reid *et al.*), 658 (f)
Herniotomy and orchidopexy; comparison of two regional techniques for postoperative analgesia in children following (Cross & Barrett), 845
High frequency jet ventilation and arterial to end tidal carbon dioxide difference (Shankar), 1124 (c)
High frequency jet ventilation for bilateral bullectomy (McCarthy *et al.*), 411
High frequency jet and conventional ventilation, comparison of cardiovascular and respiratory function during, for one lung anaesthesia (Jenkins *et al.*), 938
High frequency jet ventilation, displacement of a minitracheotomy tube during (Ravalia & Stockwell), 1306
High frequency jet ventilation, insertion of intratracheal stents (Sherry *et al.*), 61
High frequency jet ventilation compared with intermittent positive pressure ventilation; haemodynamic effects, studies following valvular heart surgery (Sherry, Windsor & Feneck), 1276
High frequency jet ventilation compared with intermittent positive pressure ventilation; studies following aortocoronary bypass graft surgery (Normandale *et al.*), 824
High frequency jet ventilation, unilateral, combined with contralateral intermittent positive pressure ventilation (Morgan *et al.*), 975
High frequency ventilation and afferent vagal activity (Harrop-Griffiths, Chakrabarti & Whitwam), 1162
Hip surgery, nerve blocks for (Rice & Pither: Smith & Allison), 1016 (c)
Histamine levels and cardiovascular responses during splenectomy and splenorenal shunt formation in a patient with systemic mastocytosis (Smith *et al.*), 861
Histamine release, basophil; allergy to suxamethonium (Withington *et al.*), 850
History: Brünings' bronchoscopic mask (Condon), 996
History of the new generation gelatins (Saddler & Horsey), 998
History: Sir Ivan Magill, a supplementary bibliography (Condon), 1096
Hormone plasma measurements following midazolam administration (Kertész), 562 (c)
Humidification by filters (Kent: Allt-Graham, Gallagher & Strangeways), 1119 (c)
Humidifier-induced hypercarbia (Raju & Olsson), 672 (c)
Hydromophone, epidural, delayed respiratory arrest after (Wüst & Bromage), 404
Hypercarbia, humidifier-induced (Raju & Olsson), 672 (c)

Hypercholinesterasaemia and suxamethonium resistance (Warran *et al.*), 855

Hyperkalaemia and cold injury (Martyn & Goldhill), 561 (c)

Hypernatraemia, gross, associated with the use of antiseptic surgical packs (Thorp, Mackenzie & Simpson), 750

Hypernatraemia, gross, associated with the use of antiseptic surgical packs (Wise: Thorp, MacKenzie & Simpson), 1331 (c)

Hyperpyrexia, malignant, suspected, propofol infusion for coronary artery bypass surgery in a patient with (Richardson), 1125 (c)

Hypertension during anaesthesia with monoamine oxidase inhibitors (Sides), 633

Hypertensive patients, beta-blocker treated, intranasal nitroglycerine attenuates pressor response to tracheal intubation in (Grover *et al.*), 884 (f)

Hypoglycaemic encephalopathy following surgery on phaeochromocytoma (Channa *et al.*), 1298

Hypophosphataemia (Lindsay & Mason), 439 (c)

Hypotension and bradycardia in spinal anaesthesia (Hutter), 89 (c)

Hypotension, prolonged, following intravenous guanethidine block (Sharpe, Milaszkiewicz & Carli), 1081

Hypotension, prolonged, after neostigmine administration in a patient receiving atenolol (Eldor, Hoffman & Davidson), 1294

Hypotension, induced, and acute beta-adrenoreceptor blockade (Simpson *et al.*), 243

Hypotension, technique to reduce incidence of; loading dose for continuous infusion epidural analgesia (MacLeod *et al.*), 377

Hypotensive anaesthesia for middle ear surgery (Williamson: Eltringham & Fairbairn), 669 (c)

Hypothermia, accidental, severe, treatment using the Clinitron bed (Miles & Thompson), 415

Hypothermia, accidental, treatment with the Clinitron bed (Lloyd; Miles & Thompson), 1121 (c)

Ilio-inguinal nerve block compared with wound infiltration for postoperative analgesia; day case herniotomy in children (Reid *et al.*), 658 (f)

Immunological reaction to glycine?; a red patient (Moskovits, Riches & Soni), 692

Infants, intratracheal pressure during controlled ventilation in (Drummond: Synnott, Wren & Davenport), 1332 (c)

Infants, peak intratracheal pressure during controlled ventilation in; computer study of the Servo 900C ventilator (Synnott, Wren & Davenport), 719

Infant, prolonged neuromuscular blockade in (Sinclair *et al.*), 1020 (c)

Infant, 4.8-kg, 5-month, management of; retrograde intubation (Cooper & Murray-Wilson), 1197

Infection risk from water bath blood warmers (Bray), 778 (c)

Infusion of atracurium, a simple system; feedback control of neuromuscular blockade (Wait, Goat & Blogg), 1212

Infusor, pneumatic pressure, loading frame for (Norley), 566 (c)

Inhalation, rapid, induction (Galloway: Wilton & Thomas), 772 (c)

Injection speed and spread of bupivacaine in the epidural space (Griffiths *et al.*), 160

Inotrope, ketamine infusion used as, in a critically ill patient (Park *et al.*), 980

Intensive care, alfentanil by intravenous infusion as long-term sedation in (Cohen & Kelly), 545 (f)

Intensive care management for removal of a giant ovarian cyst (Morrison & Morgan), 965

Intensive care unit, one year's experience with the APACHE II severity of disease classification system (Jacobs, Chang & Lee), 738

Intensive care, propofol infusion for sedation (Newman *et al.*), 929

Intensive care, a way forward for (Branthwaite: Browne: Hinds: Willatts & Searle: Blakeley: Stoddart: Major), 550 (c)

Intensive therapy unit, vecuronium infusions in patients with renal failure in (Smith, Hunter & Jones), 387

Interaction, monoamine oxidase inhibitor/tricyclic, fatal disseminated intravascular coagulation following (Tackley & Tregaskis), 760

Intercostal catheterisation, an alternative approach to the paravertebral space (Mowbray, Wong & Murray), 958

Intercostal nerve blockade for children (Shelly & Park), 541 (f)

Intercostal nerve blocks, upper limb sympathetic blockade following (Purcell-Jones, Speedy & Justins), 984

Intermittent positive pressure ventilation, bowel sounds during (Shelly & Church), 207 (c)

Intermittent positive pressure ventilation compared with high frequency jet ventilation, haemodynamic effects; studies following valvular heart surgery (Sherry, Windsor & Feneck), 1276

Intermittent positive pressure ventilation compared with high frequency jet ventilation, studies following aortocoronary bypass graft surgery (Normandale *et al.*), 824

Intermittent positive pressure ventilation, contralateral, combined with unilateral high frequency jet ventilation (Morgan *et al.*), 975

International congress calendar, 116, 457, 795, 1147

International Malignant Hyperpyrexia Workshop, 4th Report of a meeting, 206

International standards, deviations from (Shankar), 444 (c)

Interview method affects incidence of postoperative sore throat (Harding & McVey), 1104 (f)

Intra-abdominal surgery, bradycardia during; modification by pre-operative anticholinergic agents (Coventry, McMenemin & Lawrie), 835

Intra-arterial injection, accidental, of propofol (Chong & Davis), 781 (c)

Intramuscular buprenorphine versus epidural sufentanil for postoperative analgesia (Donadoni & Rolly), 1171

Intramuscular premedication, the respiratory depressant effects of nalbuphine and papaveretum as (Rutter, Aveling & Tusiewicz), 1176

Intranasal nitroglycerine attenuates pressor response to tracheal intubation in beta-blocker treated hypertensive patients (Grover *et al.*), 884 (f)

Intra-ocular pressure in adults, a comparison between the effects of fentanyl, droperidol with fentanyl, and halothane anaesthesia on (Feneck & Durkin), 266

Intra-ocular pressure control during the induction of anaesthesia for emergency eye surgery; a high-dose vecuronium technique (Abbott & Samuel), 1008 (f)

Intra-ocular pressure, effects of vecuronium (Mirakhur *et al.*), 944

Intra-ocular pressure in young children, and anaesthesia; study of three different techniques of anaesthesia (Dear *et al.*), 259

Intra-operative myocardial ischaemia (Griffin: Davis), 1127 (c)

Intrathecal morphine in aortic aneurysm surgery (Davis), 491

Intrathecal opioids, respiratory depression after; long-term epidural opioid therapy (Krantz & Christensen), 168

Intratracheal peak pressure during controlled ventilation in infants and children; computer study of the Servo 900C ventilator (Synnott, Wren & Davenport), 719

Intratracheal pressure during controlled ventilation in infants (Drummond: Synnott, Wren & Davenport), 1332 (c)

Intratracheal stents, insertion of; anaesthetic management using high frequency jet ventilation or cardiopulmonary bypass (Sherry *et al.*), 61

Intravenous anaesthesia, a new steroid preparation, pregnanolone emulsion, for; an experimental study in mice (Høgskilde *et al.*), 586

Intravenous cannulae, flow through (Kestin), 67

Intravenous cyproheptadine and carcinoid syndrome (Solares *et al.*), 989

Intravenous feeding, an unusual complication of, in the presence of a mediastinal abscess; atriobronchial fistula (Graziotti), 669 (c)

Intravenous guanethidine block, a case of prolonged hypotension following (Sharpe, Milaszkiewicz & Carli), 1081

Intravenous infusion of alfentanil as long-term sedation in intensive care (Cohen & Kelly), 545 (f)

Intravenous infusion systems, pressure–flow relationships in (Philip & Philip: Kestin), 775 (c)

Intravenous injections (Tweedie), 1339 (c)

Intravenous injections, pain-free (Porteous), 1021 (c)

Intravenous isosorbide dinitrate, acute effects of, during cardiac surgery (Parsons, Wetzel & Mohandas), 498

Intravenous morphine and nalbuphine, gastric emptying and small bowel transit times in volunteers after (Yukioka *et al.*), 704

Intravenous regional analgesia, pneumatic tourniquet paralysis following (Larsen & Hommelgaard), 526

Intravenous sedation for cataract surgery (Gilbert *et al.*), 1063

Intravenous sedation, propofol for (Mackenzie & Grant), 3

Intravenous versus tracheal atropine; comparison of the effects on heart rate (Bray, Jones & Grundy), 1188

Intubation, bronchial, selective (Welsh), 82 (c)

Intubation, difficult, bronchial (Russell, Frazer & Richardson), 82 (c)

Intubation, difficult, bronchial (Skinner), 567 (c)

Intubation, difficult, complications of (Mostafa), 1241 (c)

Intubation, difficult, a laryngoscope adaptor for (Yentis), 764

Intubation, difficult, a new laryngoscope to facilitate intubation in cases of restricted access (Nunn), 877

Intubation, difficult, Macintosh laryngoscope modification for (Callander & Thomas), 771 ((c)

Intubation, difficult, nasal (Sansome), 209 (c)

Intubation, difficult, tracheal (Sellers & Yogendran), 1243 (c)

Intubation, difficult, tracheal, cellulitis as a complication of (Young & Robinson), 569 (c)

Intubation, difficult, tracheal, modified Magill forceps for (Vonwiller, Liberman & Maver), 777 (c)

Intubation, difficult, tracheal, due to tracheopathia osteochondroplastica (Smith, Pillai & Gillbe), 536

Intubation, difficult, unexpected (Millar), 1021 (c)

Intubation, difficult, unexpected; asymptomatic epiglottic cysts as a cause of upper airway obstruction during anaesthesia (Mason & Wark), 407

Intubation, difficult, visibility of pharyngeal structures as a predictor of (Charters, Perera & Horton: Young), 115 (c)

Intubation, fibreoptic, transillumination in (Whitlock & Calder), 570 (c)

Intubation, nasal (Webb), 329 (c)

Intubation, nasotracheal, another approach (Mehta), 1126 (c)

Intubation, nasotracheal, a problem with another approach (Kuwelker & Lawler), 442 (c)

Intubation, nasotracheal, traumatic (Thomas), 573 (c)

Intubation, retrograde; management of a 4.8-kg, 5-month infant (Cooper & Murray-Wilson), 1197

Intubation, tracheal, difficult, modified Magill forceps for (Pelimon & Simunovic), 83 (c)

Intubation, tracheal, failed, propofol in (Coleman & Phillips), 1233 (c)

Isoflurane for anaesthesia in the dental chair; a comparison of the incidence of cardiac dysrhythmias during anaesthesia with halothane and isoflurane (Cripps & Edmondson), 189 (f)

Isoflurane anaesthesia for laparoscopy; comparison with propofol, etomidate and thiopentone (de Grood *et al.*), 815
Isoflurane compared with enflurane anaesthesia; serum fluoride levels in morbidly obese patients (Strube, Hulands & Halsey), 685
Isoflurane compared with halothane and trichloroethylene; a study of drawover air anaesthesia with the Triservice anaesthetic apparatus (Tighe & Pethybridge), 887 (f)
Isoflurane, recovery from, comparison with propofol infusion as the main agent for outpatient arthroscopy (Zuurmond, van Leeuwen & Helmers), 356
Isoflurane day case anaesthesia, comparison of propofol and methohexitone as induction agents (O'Toole *et al.*), 373
Isoflurane in a drawover anaesthesia system (Yoganathan & Houghton), 1241 (c)
Isoflurane and enflurane as alternatives to halothane; Triservice anaesthetic apparatus (Kocan), 1101 (f)
Isoflurane and halothane anaesthesia in the dental chair, a comparison of the incidence of cardiac dysrhythmias (Cripps & Edmondson), 189 (f)
Isoflurane, respiratory effects of, in spontaneously breathing children (Murat *et al.*), 711
Isosorbide dinitrate, intravenous, acute effects of, during cardiac surgery (Parsons, Wetzel & Mohandas), 498

Jackson–Rees modification of Ayre's T-piece, an antipollution device for use with (Paul), 439 (c)
Jackson–Rees modification of the Ayre's T-piece, improved antipollution device for (Spargo, Apadoo & Wilton), 1240 (c)
Jehovah's Witness, severe acute anaemia; survival without blood transfusion (Howell & Bamber), 44
Jet ventilators, hazard of silencers for (Van Besouw), 81 (c)

Kaye, Dr Geoffrey (Wilson), 426 (c)
Ketamine infusion, use as a sedative, inotrope and bronchodilator in a critically ill patient (Park *et al.*), 980
Ketamine and morphine infusions for postoperative analgesia, a comparison (Owen *et al.*), 1051
Ketorolac tromethamine, morphine sparing effect of; study of new, parenteral non-steroidal anti-inflammatory agent after abdominal surgery (Gillies *et al.*), 727
Kinked pilot tube (Tanski & James), 1022 (c)
Kinked pilot tube, difficult extubation due to (Mehta), 443 (c)
Kinked tube or bronchospasm? (Ross), 441 (c)

Labelling error (Bickford-Smith & Evans; Wood), 572 (c)
Labour and delivery, management in a patient with Guillain–Barré syndrome (McGrady), 899 (c)
Labour, epidural catheter migration during (Phillips & Macdonald), 661 (f)
Labour, an epidural infusion technique for (Gaylard, Wilson & Balmer), 1098 (f)
Labour, pethidine compared with meptazinol during; a prospective randomised double-blind study (Morrison *et al.*), 7
Labour, pethidine compared with nalbuphine for pain relief in, when administered by patient-controlled analgesia (Frank *et al.*), 697
Laparoscopy, anaesthesia, a comparison of five techniques including propofol, etomidate, thiopentone and isoflurane (de Grood *et al.*), 815
Laryngeal placement confirmed by bimanual tactile examination of positioned orotracheal tube (Charters & Wilkinson), 801
Laryngeal reflexes, comparison of effects of lormetazepam and Diazemuls (Groves, Rees & Rosen), 808
Laryngoscope adaptor for difficult intubation (Yentis), 764
Laryngoscope, Macintosh, modification for difficult intubation (Callander & Thomas), 671 (c)
Laryngoscope, new, modified, to facilitate intubation in cases of restricted access (Nunn), 877
Larynx, pharynx and trachea, transnasal anaesthesia of (Kartha & Cyriac-Mathew), 320 (c)
Laser bronchoscopy, carbon dioxide, a review of problems and complications (Conacher, Paes & Morritt), 511
Laser, carbon dioxide, surgery in tracheobronchial lesions; anaesthetic management (Hunton & Oswal), 1222 (f)
Lateral decubitus position, unilateral pulmonary oedema/atelectasis in (Baraka, Moghrabi & Yazigi), 171
Lavage, epidural, for extensive epidural suppuration (Cardan & Nanulescu), 1023 (c)
Lead systems compared using computerised ST segment analysis; myocardial ischaemia during non-cardiac surgery (Griffin & Kaplan), 155
Leak detection with a capnograph (Martin), 1025 (c)
Leak, oxygen, preferential; an unusual case (Hanning, Kruchek & Chunara: Sim), 1329 (c)
Leaks, potential, from anaesthetic machines, through open Rotameter valves and empty cylinder yokes (McQuillan & Jackson), 1308
Leasing, of equipment (Wauchob), 219 (c)
Ligation, *see* Tubal ligation
Lignocaine, hyperbaric, subarachnoid block with; comparison with hyperbaric bupivacaine (Ewart & Rubin), 1183
Lignocaine/etomidate, angioneurotic oedema following (Bricker & Raitt), 323 (c)
Lignocaine pretreatment, effect on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Lithotripsy, shock wave, extracorporeal (Economacos *et al.*), 779 (c)

Liver grafting, the prevention of renal impairment in patients undergoing, by infusion of low dose dopamine (Polson *et al.*), 15
Liver tumours and muscle relaxants; electromyographic studies in children (Brown *et al.*), 1284
Loading dose for continuous infusion epidural analgesia; technique to reduce the incidence of hypotension (MacLeod *et al.*), 377
Loading frame for pneumatic pressure infusor (Norley), 566 (c)
Local anaesthetic blocks in children, simple device for assessment of (Cross), 84 (c)
Local tissue oxygenation following radial artery cannulation (Murray & Mowbray), 1070
Lorazepam in a fast dissolving dose form as a premedicant for children (Underhill, Bush & Harper), 319 (c)
Lormetazepam and Diazemuls, comparison of their effects on laryngeal reflexes (Groves, Rees & Rosen), 808
Lung and heart transplantation, combined, anaesthesia for (Sale *et al.*), 249
Lung, one, anaesthesia; cardiovascular and respiratory function compared during conventional ventilation and high frequency jet ventilation (Jenkins *et al.*), 938
Lung, total collapse, and CPAP (Davies & Grant), 780 (c)
Lung water during the puerperium (MacLennan, MacDonald & Campbell), 141
Lupus anticoagulant, implications for obstetric anaesthetists (Malinow *et al.*), 1291

Macintosh laryngoscope, modification for difficult intubation (Callander & Thomas), 671 (c)
Magill, Sir Ivan Whiteside: editorial (Edridge), 231
Magill, Sir Ivan, a supplementary bibliography (Condon), 1096
Magill forceps, modified, for difficult tracheal intubation (Pelimon & Simunovic), 83 (c)
Magill forceps, modified, for difficult tracheal intubation (Vonwiller, Liberman & Maver), 777 (c)
Magill versus Mallinckrodt tracheal tubes, comparative study of postoperative sore throat (Sprague & Archer), 306 (f)
Magnesium trisilicate mixture, BP, carminative property of peppermint in (Robson), 776 (c)
Malignant hyperpyrexia, suspected; propofol infusion for coronary artery bypass surgery in a patient with (Richardson), 1125 (c)
Malignant Hyperpyrexia Workshop, 4th International, report of a meeting, 206
Mallinckrodt versus Magill tracheal tubes, comparative study of postoperative sore throat (Sprague & Archer), 306 (f)
Marcain ampoule, contaminated (Sugden & Bembridge: Watson), 87 (c)
Marcain shakes (Dow & Wilkins), 328 (c)
Mask, bronchoscopic, Brünings' (Condon), 996
Maternal propofol administration, prolonged, absence of clinically significant neonatal respiratory depression after (Bloor, Jones & Turner), 1233 (c)
Maternity Services Liaison Committees and the anaesthetist (Owen), 894 (c)
Mediastinal abscess; atriobronchial fistula, an unusual complication of intravenous feeding in the presence of (Graziotti), 669 (c)
Memory of cardiac anaesthesia; psychological sequelae in cardiac patients of intra-operative suggestion and operating room conversation (Goldmann, Shah & Hebden), 596
Menstrual cycle and severe acute asthma (Lenoir), 1287
Meptazinol, epidural (Rao *et al.*), 218 (c)
Meptazinol compared with pethidine during labour, a prospective randomised double-blind study (Morrison *et al.*), 7
Metabolism, midazolam, failure of, in critically ill patients (Shelly, Mendel & Park), 619
Methohexitone anaesthesia, effect of low dose sufentanil pretreatment (Furness, Dundee & Milligan), 1264
Methohexitone and propofol compared for day case isoflurane anaesthesia (O'Toole *et al.*), 373
Mice, an experimental study of pregnanolone emulsion in (Høgskilde *et al.*), 586
Microlaryngeal surgery, comparison of etomidate and propofol anaesthesia (de Grood *et al.*), 366
Midazolam administration, plasma hormone measurements following (Kertész), 562 (c)
Midazolam anaesthesia, effect of low dose sufentanil pretreatment (Furness, Dundee & Milligan), 1264
Midazolam anaesthetic properties, comparison with pregnanolone emulsion (Høgskilde *et al.*), 1045
Midazolam, a comparison of the early pharmacokinetics in pregnant and nonpregnant women (Wilson *et al.*), 1057
Midazolam, failure of critically ill patients to metabolise (Shelly, Mendel & Park), 619
Midazolam, oral, for premedication in day case surgery (Raybould & Bradshaw), 591
Midazolam pretreatment, effect of serum myoglobin, creatine kinase and myalgia (Laurence), 503
Migration, epidural catheter, during labour (Phillip & Macdonald), 661 (f)
Miller's syndrome; anaesthetic management of postaxial acrofacial dysostosis (Richards), 871
Minitracheostomy (Boykett), 87 (c)
Minitracheostomy (Wagstaff, Sparling & Ryan), 216 (c)
Minitracheostomy—a modified procedure (Willis), 216 (c)
Minitracheotomy, re-insertion of (Stokes), 782 (c)
Minitracheotomy tube, displacement during high frequency jet ventilation (Ravalia & Stockwell), 1306
Minitracheotomy tube, misplacement (Tran & Hedley), 783 (c)

Monitoring, minimal, and vigilance: editorial (Mathias & Lunn), 683
Monitoring neuromuscular blockade; the table knife transducer (Dundas, Levack & Brockway), 1092
Monoamine oxidase inhibitors, hypertension during anaesthesia with (Sides), 633
Monoamine oxidase inhibitor/tricyclic interaction, fatal disseminated intravascular coagulation following (Tackley & Tregaskis), 760
Morbidity and early retirement among anaesthetists and other specialists (McNamee, Keen & Corkill), 133
Morbidity and early retirement (Adams: Hutchinson: Keen & McNamee), 1024 (c)
Morbidly obese patients, serum fluoride levels in; enflurane compared with isoflurane anaesthesia (Strube, Hulands & Halsey), 685
Morphine administration, epidural, chronic, in a cancer patient, spinal cord compression during (van Diejen, Driessen & Kaanders), 1201
Morphine, intrathecal, in aortic aneurysm surgery (Davis), 491
Morphine and ketamine infusions for postoperative analgesia, a comparison (Owen *et al.*), 1051
Morphine and nalbuphine, intravenous, gastric emptying and small bowel transit times in volunteers after (Yukioka *et al.*), 704
Morphine sparing effects of diclofenac sodium following abdominal surgery (Hodsman *et al.*), 1005 (f)
Morphine sparing effect of ketorolac tromethamine; study of new, parenteral non-steroidal anti-inflammatory agent after abdominal surgery (Gillies *et al.*), 727
Morphine tablets, controlled release, a double-blind trial in patients with advanced cancer (Hanks, Twycross & Bliss), 840
Morphine-induced respiratory depression in the elderly (Bourke: Bowen *et al.*), 428 (c)
Muscle relaxants, economy in the use of; vecuronium after pancuronium (Kay *et al.*), 277
Muscle relaxants and liver tumours; electromyographic studies in children (Brown *et al.*), 1284
Myalgia and biochemical changes following intermittent suxamethonium administration; effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Myasthenia gravis, suxamethonium in (Wainwright & Brodrick), 950
Myocardial ischaemia during non-cardiac surgery; a comparison of different lead systems using computerised ST segment analysis (Griffin & Kaplan), 155
Myocardial ischaemia, intra-operative (Griffin: Davis), 1127 (c)
Myoglobin, serum, effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on (Laurence), 503

Nalbuphine and morphine, intravenous; gastric emptying and small bowel transit times in volunteers after (Yukioka *et al.*), 704
Nalbuphine and papaveretum as intramuscular premedication, the respiratory depressant effects of (Rutter, Aveling & Tusiewicz), 1176
Nalbuphine for obstetric analgesia; a comparison of nalbuphine with pethidine for pain relief in labour when administered by patient-controlled analgesia (PCA) (Frank *et al.*), 697
Narcoanalgesia (Fortuna), 329 (c)
Narcotics, action on the pupil (Larson), 566 (c)
Nasal adhesion following prolonged nasotracheal intubation (Sherry & Murday), 561
Nasal intubation (Webb), 329 (c)
Nasal intubation, difficult (Sansome), 209 (c)
Nasotracheal intubation, another approach (Mehta), 1126 (c)
Nasotracheal intubation; a problem with another approach (Kuwelker & Lawler), 442 (c)
Nasotracheal intubation, a nasal adhesion following (Sherry & Murday), 651
Nasotracheal intubation, traumatic (Thomas), 573 (c)
Nausea and vomiting after prostaglandins in day case termination of pregnancy; the efficacy of low dose droperidol (Millar & Hall), 613
Nebules, ventolin (Mackie), 1332 (c)
Nebulised adrenaline (Gwinnutt & Lord: Choudhry: Child: Meakin & Remington), 320 (c)
Nebulised adrenaline, croup and preservatives (Hinton & Goss), 436 (c)
Needle, epidural, *in vitro* study of the effect of rotation (Meiklejohn), 1180
Needlestick injury from indwelling steel needle (Kinsella), 900 (c)
Neonatal respiratory depression, clinically significant, absence of, after prolonged maternal propofol administration (Bloor, Jones & Turner), 1233 (c)
Neonates, analgesia for (Gauntlett), 1328 (c)
Neonates, use of opioids in; a retrospective study of 933 cases (Purcell-Jones, Dormon & Sumner), 1316 (f)
Neonates, postoperative analgesia; editorial (Booker), 343
Neostigmine administration, prolonged bradycardia and hypotension after, in a patient receiving atenolol (Eldor, Hoffman & Davidson), 1294
Nerve blocks for hip surgery (Rice & Pither: Smith & Allison), 1016 (c)
Nerve block, ilio-inguinal, compared with wound infiltration for postoperative analgesia; day case herniotomy in children (Reid *et al.*), 658 (f)

Nerve palsy occurring during the recovery period (Hughes-Davies), 326 (c)
Nerve stimulator, low-power, use during sciatic nerve block (Smith & Allison), 296
New World, use of volatile anaesthetics in (Strunin & Davies), 774 (c)
News and Notices, 105, 924, 1152
Newtons, SI units and apples (Rye), 1025 (c)
Neuroanaesthesia tracheal tubes, latex rubber, nylon reinforced (Wright & Mundy), 1012 (f)
Neurofibromatosis, upper airway obstruction in (Crozier), 1209
Neuroleptic malignant syndrome, case report with a review of the literature (Allsop & Twigley), 49
Neuromuscular blockade, feedback controls; a simple system for infusion of atracurium (Wait, Goat & Blogg), 1212
Neuromuscular blockade, monitoring; the table knife transducer (Dundas, Levack & Brockway), 1092
Neuromuscular blockade, prolonged, in an infant (Sinclair *et al.*), 1020 (c)
Neuromuscular blockade, prolonged, in a patient with a normal genotype (Cherala: Sapsford & Bush), 214 (c)
Neuromuscular blockade, steady-state, during surgery, using a computer controlled closed-loop atracurium infusion (Webster & Cohen), 1085
Neuromuscular blocking effect of vecuronium, prolongation by antibiotics (Jedeikin *et al.*), 858
Nitroglycerine, intranasal, attenuates pressor response to tracheal intubation in beta-blocker treated hypertensive patients (Grover *et al.*), 884 (f)
Nitroprusside and beta blockade (Coad; Simpson), 1022 (c)
Nitrous oxide and hearing loss (Coe), 1230 (c)
Nitrous oxide and oxyhaemoglobin dissociation (Runciman *et al.*), 894 (c)
Nitrous oxide does not alter oxyhaemoglobin dissociation in dog or man (Powers & Artru), 668 (c)
Nitrous oxide and pregnancy (Nunn: Mazze), 427 (c)
Nitrous oxide in early pregnancy (Keeling), 211 (c)
Nitrous oxide and relaxant anaesthesia, comparison of trichloroethylene and enflurane as adjuncts to (Rice & Reynolds), 1320 (f)
Nitrous oxide–oxygen, propofol combined with, for induction and maintenance of anaesthesia (Herregods *et al.*), 360
Nitrous oxide–oxygen, should it be replaced by air–oxygen in general anaesthesia? (Moseley *et al.*), 609
Nomenclature of circle absorption breathing systems (Horsey: Twigley, Chakrabarti & Whitwam), 1018 (c)
Non vagolytic anaesthetic sequence—sinus arrest (Thorp & Higgins), 432 (c)
Normac analyser and alcohol vapour (Yamashita & Tsuneto), 209 (c)
Nuffield 200 ventilator, another modification (Kwan & See: Calhaem), 80 (c)

Obese patients, morbidly, serum fluoride levels in; enflurane compared with isoflurane anaesthesia (Strube, Hulands & Halsey), 685
Obese patient, morbidly, propofol in (Kirby & Howard), 1125 (c)
Obesity index, Bain anaesthetic system and gender (Shankar *et al.*), 779 (c)
Obituaries
  Barnsley, A., 1147
  Challenger, J. H. 1147
  Conway, C. M., 105
  Downing, D., 1147
  Dunnill, D. E., 457
  Gergis, L. A., 457
  Gilmartin, T. J., 105
  Hammerton-Fraser, A. M., 457
  Hargadon, J. J., 1147
  Knight, R. F., 795
  Lake, R. H. N., 1147
  Mather, L., 1147
  Merlin, P. T., 1147
  Moran, J. L. C., 457
  Patterson, W. J., 1147
  Roper, R. E., 795
  Spratt, L. W., 1147
  Steen, T. R., 1147
  Steward, A. M., 1147
  Thomas, R. T., 1147
  Todd, C. G., 457, 795
Obstetric anaesthetists, implications of lupus anticoagulant for (Malinow *et al.*), 1291
Obstetric analgesia, nalbuphine for; comparison with pethidine for pain relief in labour when administered by patient-controlled analgesia (Frank *et al.*), 697
Obstetric epidural test doses (Cartwright), 556 (c)
Obstetrics, priming with vecuronium in (Cherala *et al.*), 1021 (c)

Obstetric units, protocols in; their use in Wales in 1983 (Owen), 1323 (f)
Oculocardiac reflex and ventilation (Blanc: Mirakhur & Jones), 324 (c)
Oculocardiac reflex, a variation; bradycardia during elevation of zygomatic fractures (Shearer & Wenstone), 1207
Oculogyric crisis after day case anaesthesia (Dingwall), 565 (c)
Oddi, spasm of the sphincter of, can be avoided (Vatashsky & Haskel), 564 (c)
Oedema, angioneurotic, following etomidate/lignocaine (Bricker & Raitt), 323 (c)
Oesophageal stethoscope (O'Dea & Hall), 1337 (c)
Old people, spontaneous ventilation in (Keen), 568 (c)
Ondine's curse and the anaesthetist (Mather), 394
Operating room conversation and intra-operative suggestion, psychological sequelae in cardiac patients; memory of cardiac anaesthesia (Goldmann, Shah & Hebden), 596
Ophthalmic anaesthesia, vomiting following (van den Berg: Mostafa & Lockhart), 897 (c)
Ophthalmic surgery, vomiting after; effects of intra-operative antiemetics and postoperative oral fluid restriction (van den Berg *et al.*), 270
Ophthalmic *see also* Eye
Opioids, intrathecal; respiratory depression after long-term epidural opioid therapy (Krantz & Christensen), 168
Opioids, use in neonates, a retrospective study of 933 cases (Purcell-Jones, Dormon & Sumner), 1316 (f)
Opisthotonos again (Cameron), 1124 (c)
Oral midazolam for premedication in day case surgery (Raybould & Bradshaw), 591
Oral surgery, influence of premedication on the occurrence of dysrhythmias during (Smith & O'Connell), 882 (f)
Orchidopexy and herniotomy, comparison of two regional techniques for postoperative analgesia in children following (Cross & Barrett), 845
Orotracheal tactile tube placement test; bimanual tactile examination of the positioned orotracheal tube to confirm laryngeal placement (Charters & Wilkinson), 801
Outpatient arthroscopy, recovery from propofol infusion as the main agent for; comparison with isoflurane (Zuurmond, van Leeuwen & Helmers), 356
Ovarian cyst, giant, removal of; anaesthetic and intensive care management (Morrison & Morgan), 965
Oxford region, the prevalence of serological markers for hepatitis B virus infection amongst anaesthetists in (Sinclair, Ashby & Kurtz), 30
Oximeter, pulse; an early warning device? (Mason), 784 (c)
Oximeter, pulse, erroneous activation (Norley: Taylor), 1116 (c)
Oximetry during transport (Finfer & Wishaw), 900 (c)
Oxygen analysers, evaluation of (Hunsley: Roe, Tyler & Barnes), 1127 (c)
Oxygen analysers, an evaluation of five fuel cell models (Roe *et al.*), 175
Oxygen–air mixtures (White: Moseley, *et al.*), 1336 (c)
Oxygen–air, should be replace nitrous oxide–oxygen in general anaesthesia? (Moseley *et al.*), 609
Oxygen concentration, inspired, determining factors in drawover anaesthetic systems (Mackie), 299
Oxygen desaturation, arterial, during postoperative transportation; the influence of operation site (Meiklejohn *et al.*), 1313 (f)
Oxygen leak, preferential, an unusual case (Hanning, Kruchek & Chunara: Sim), 1329 (c)
Oxygen–nitrous oxide, propofol combined with, for induction and maintenance of anaesthesia (Herregods *et al.*), 360
Oxygen saturation, arterial, during general anaesthesia for paediatric dental extractions (Bone, Galler & Flynn), 879 (f)
Oxygenation during electroconvulsive therapy (Wood: Sneyd: Hanning, Lew & Eastley), 431 (c)
Oxygenation during electroconvulsive therapy (Simpson, Chater & Swindells: Hanning, Lew & Eastley), 1234 (c)
Oxygenation, local tissue, after radial artery cannulation (Murray & Mowbray), 1070
Oxyhaemoglobin dissociation and nitrous oxide (Runciman *et al.*), 894 (c)
Oxyhaemoglobin dissociation is not altered by nitrous oxide, in dog or man (Powers & Artru), 668 (c)

Paediatric anaesthesia, manufactured drug dilutions for (Laishley), 213 (c)
Paediatric dental extractions, arterial oxygen saturation during general anaesthesia for (Bone, Galler & Flynn), 879 (f)
Paediatric wedge, inflatable (Bembridge), 213 (c)
Pain, chronic, depression and anxiety (Jack *et al.*), 1235 (c)
Pain, postoperative, management with few side effects; large dose epidural sufentanil (Madej, Watson & Martin), 1204
Pain-free intravenous injections (Porteous), 1021 (c)
Palsy, nerve, occurring during the recovery period (Hughes-Davies), 326 (c)
Pancuronium, with and without glycopyrronium, and bradycardia; comparison with vecuronium (Cozanitis, Pouttu & Rosenberg), 192 (f)
Pancuronium, alcuronium and phaeochromocytoma (Solares *et al.*), 77 (c)
Pancuronium and renal failure (Sangala & Dixon: Hunter), 1236 (c)
Pancuronium, vecuronium after; economy in the use of muscle relaxants (Kay *et al.*), 277

Papaveretum and nalbuphine as intramuscular premedication, the respiratory depressant effects of (Rutter, Aveling & Tusiewicz), 1176
Paralysis, pneumatic tourniquet, following intravenous regional analgesia (Larsen & Hommelgaard), 526
Paralysis, prolonged, following an infusion of alcuronium in a patient with renal dysfunction (Smith, Hunter & Jones), 522
Paroxysmal nocturnal haemoglobinuria; peri-operative management of a patient with Budd–Chiari syndrome (Taylor, Whitwam & Worsley), 639
Parturient patient, and pre-oxygenation (Russell *et al.*), 346
Patient-controlled analgesia, a comparison of nalbuphine with pethidine for pain relief in labour when administered by (Frank *et al.*), 697
Patients with problems (Nott: Frost), 328 (c)
Penlon off-line vaporizer mounting system, another hazard with (Woollam), 781 (c)
Peppermint in magnesium trisilicate mixture, BP, carminative property of (Robson), 776 (c)
Percutaneous infraclavicular approach, new, to the axillary vein (Nickalls), 151
Peri-operative administration of a somatostatin analogue to suppress carcinoid tumour activity (Roy, Carter & Wright), 627
Peri-operative fluids (Bennett: Hillman), 570 (c)
Peri-operative management of a patient with Budd–Chiari syndrome; paroxysmal nocturnal haemoglobinura (Taylor, Whitwam & Worsley), 639
Perivascular and nerve stimulator techniques, comparison of success rate of axillary brachial plexus block using (Tuominen *et al.*), 20
Pethidine compared with meptazinol during labour, a prospective randomised double-blind study (Morrison *et al.*), 7
Pethidine compared with nalbuphine for pain relief in labour when administered by patient-controlled analgesia (Frank *et al.*), 697
Phaeochromocytoma, alcuronium and pancuronium (Solares *et al.*), 77 (c)
Phaeochromocytoma as a cause of pulmonary oedema (Blom *et al.*), 646
Phaeochromocytoma, hypoglycaemic encephalopathy following surgery on (Channa *et al.*), 1298
Pharmacodynamics and stability of diamorphine (Hanks, Hoskin & Walker), 664 (c)
Pharmacokinetics, early, of midazolam, a comparison in pregnant and nonpregnant women (Wilson *et al.*), 1057
Pharyngeal structure visibility as a predictor of difficult intubation (Charters, Perera & Horton: Young), 1115 (c)
Pharynx, larynx and trachea, transnasal anaesthesia of (Kartha & Cyriac-Mathew), 320 (c)
Phenol, subtrigonal, cardiac dysrhythmia after (Forrest & Ramage), 777 (c)
Pilot tube, kinked (Tanski & James), 1022 (c)
Pilot tube, kinked, difficult extubation due to (Mehta), 443 (c)
Piriform fossa perforation during attempted tracheal intubation (Wengen), 519
Plasma hormone measurements following midazolam administration (Kertész), 562 (c)
Plasma potassium, beta-adrenoceptor blockade and suxamethonium-induced rise in (Maryniak *et al.*), 71 (f)
Plasma potassium, continuous display during cardiac surgery (Drake, Treasure & Smith), 23
Pleural aspiration with a central venous catheter (Cooper), 217 (c)
Pleural aspiration with a central venous catheter (Thorp), 896 (c)
Pneumatic pressure infusor, loading frame for (Norley), 566 (c)
Pneumatic tourniquet paralysis following intravenous regional analgesia (Larsen & Hommelgaard), 526
Pneumothorax, persistent, treated with continuous positive airway pressure (Elphinstone & Grant), 987
Positive airway pressure, continuous, treatment for persistent pneumothorax (Elphinstone & Grant), 987
Positive pressure intermittent ventilation, bowel sounds during (Shelly & Church), 207 (c)
Postaxial acrofacial dysostosis, Miller's syndrome; anaesthetic management (Richards), 871
Postmortem removal of tracheal tube (Watson: Knight & Addicott), 554 (c)
Postmortem removal of tracheal tube (Johnston & Charters), 1242 (c)
Postoperative analgesia in children following herniotomy and orchidopexy, comparison of two regional techniques (Cross & Barret), 845
Postoperative analgesia, a comparison of infusions of morphine and ketamine (Owen *et al.*), 1051
Postoperative analgesia, epidural buprenorphine for (Kumar: Wolff, Carl & Crawford), 79 (c)
Postoperative analgesia, epidural sufentanil versus intramuscular buprenorphine for (Donadoni & Rolly), 1171
Postoperative analgesia for neonates: editorial (Booker), 343
Postoperative analgesia for day case herniotomy in children, a comparison of ilio-inguinal nerve block and wound infiltration (Reid *et al.*), 658 (f)
Postoperative complications of dystrophia myotonica (Aldridge), 1121 (c)
Postoperative complications of dystrophia myotonica (Moore & Moore), 529
Postoperative complications of dystrophia myotonica (Zuck: Moore & Moore), 1023 (c)
Postoperative headache in young patients after spinal anaesthesia (Flaatten *et al.*), 202 (f)
Postoperative pain management with few side effects; large dose epidural sufentanil (Madej, Watson & Martin), 1204
Postoperative sore throat, comparison of Magill and Mallinckrodt tracheal tubes (Sprague & Archer), 306 (f)
Postoperative sore throat, interview method affects incidence of (Harding & McVey), 1104 (f)

Postoperative transportation, arterial oxygen desaturation during; the influence of operation site (Meiklejohn *et al.*), 1313 (f)
Potassium, beta blockade and suxamethonium (Goldhill & Martyn), 670 (c)
Potassium, plasma; beta-adrenoceptor blockade and suxamethonium-induced rise in (Maryniak *et al.*), 71 (f)
Potassium, plasma, continuous display during cardiac surgery (Drake, Treasure & Smith), 23
Potentials, evoked, the effect of benzodiazepines on (Milligan, Howard & Dundee: Sebel), 1237 (c)
Potentials, evoked, following diazepam or fentanyl (Loughnan *et al.*), 195 (f)
Pregnancy, early, nitrous oxide in (Keeling), 211 (c)
Pregnancy, near-term, cardiac arrest in (Lindsay & Hanson), 1074
Pregnancy and nitrous oxide (Nunn: Mazze), 427 (c)
Pregnancy, a prospective study of 200 consecutive twin deliveries (Crawford), 33
Pregnancy, effect on pulmonary nitrogen washout; a study of pre-oxygenation (Byrne, Oduro-Dominah & Kipling), 148
Pregnancy termination, day case, nausea and vomiting after prostaglandins in; the efficacy of low dose droperidol (Millar & Hall), 613
Pregnant and nonpregnant women; a comparison of the early pharmacokinetics of midazolam (Wilson *et al.*), 1057
Pregnant patients, spinal anaesthesia in (Edmondson & Erwin), 666 (c)
Pregnanolone emulsion, a new steroid preparation for intravenous anaesthesia; an experimental study in mice (Høgskilde *et al.*), 586
Pregnanolone emulsion, anaesthetic properties; comparison with alphaxolone/alphadolone, propofol, thiopentone and midazolam in a rat model (Høgskilde *et al.*), 1045
Premedicant for children; lorazepam in a fast dissolving dose form (Underhill, Bush & Harper), 319 (c)
Premedication for day case surgery; a study of oral midazolam (Raybould & Bradshaw), 591
Premedication, influence on the occurrence of dysrhythmias during oral surgery (Smith & O'Connell), 882 (f)
Premedication, intramusular, the respiratory depressant effects of nalbuphine and papaveretum as (Rutter, Aveling & Tusiewicz), 1176
Premedication, triazolam (Pinnock & Fell: Tipping, Blogg & Thomas), 316 (c)
Pre-operative carotid sinus massage, value of (McConachie), 636
Pre-operative visits (Bethune), 553 (c)
Pre-oxygenation and the parturient patient (Russell *et al.*), 346
Pre-oxygenation study; the effect of pregnancy on pulmonary nitrogen washout (Byrne, Oduro-Dominah & Kipling), 148
Preservatives, croup and nebulised adrenaline (Hinton & Goss), 436 (c)
Pressor response to tracheal intubation in beta-blocker treated hypertensive patients is attenuated by intranasal nitroglycerine (Grover *et al.*), 884 (f)
Pressures, extradural, and hanging drop (McKinney), 1132 (c)
Pressure, intratracheal, during controlled ventilation in infants (Drummond; Synnott, Wren & Davenport), 1332 (c)
Pressure, intratracheal, peak, during controlled ventilation in infants and children; computer study of the Servo 900C ventilator (Synnott, Wren & Davenport), 719
Pressure–flow relationships in intravenous infusion systems (Philip & Philip: Kestin), 775 (c)
Pretreatments, alcuronium, lignocaine, midazolam and suxamethonium, effects on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Pretreatment, low dose sufentanil, effect on induction of anaesthesia with thiopentone, methoxhexitone or midazolam (Furness, Dundee & Milligan), 1264
Prilocaine, anaphylactoid reactions to (Ruiz *et al.*), 1078
Priming with vecuronium in obstetrics (Cherala *et al.*), 1021 (c)
Prochlorperazine and vomiting after eye surgery (van den Berg & Lambourne), 898 (c)
Propofol, accidental intra-arterial injection of (Chong & David), 781 (c)
Propofol administration, maternal, prolonged, absence of clinically significant neonatal respiratory depression after (Bloor, Jones & Turner), 1233 (c)
Propofol anaesthesia for laparoscopy, comparison with etomidate, thiopentone and isoflurane (de Grood *et al.*), 185
Propofol anaesthetic properties, comparison with pregnanolone emulsion (Høgskilde *et al.*), 1045
Propofol, arousal from (Hunter, Thornily & Whitburn), 1128 (c)
Propofol combined with nitrous oxide–oxygen for induction and maintenance of anaesthesia (Herregods *et al.*), 360
Propofol and etomidate compared in microlaryngeal surgery (de Grood *et al.*), 366
Propofol in failed tracheal intubation (Coleman & Phillips), 1233 (c)
Propofol infusion, bradycardia after (Thomson & Yate), 430 (c)
Propofol infusion for coronary artery bypass surgery in a patient with suspected malignant hyperpyrexia (Richardson), 1125 (c)
Propofol infusion as the main agent for outpatient arthroscopy, recovery from; comparison with isoflurane (Zuurmond, van Leeuwen & Helmers), 356

Propofol infusion for sedation in intensive care (Newman *et al.*), 929
Propofol for intravenous sedation (Mackenzie & Grant), 3
Propofol and methohexitone compared for day case isoflurane anaesthesia (O'Toole *et al.*), 373
Propofol in a morbidly obese patient (Kirby & Howard), 1125 (c)
Propofol and thiopentone, relative potency (Grant & Mackenzie: O'Connor & Wilkinson: Grounds, Taylor & Morgan), 317 (c)
Propofol and thiopentone, relative potency (Kay), 1025 (c)
Prostaglandins in day case termination of pregnancy, nausea and vomiting after; the efficacy of low dose droperidol (Millar & Hall), 613
Prune-belly syndrome, anaesthesia in; a review of 36 cases (Henderson, Vallis & Sumner), 54
Psychological sequelae in cardiac patients of intra-operative suggestion and operating room conversation; memory of cardiac anaesthesia (Goldmann, Shah & Hebden), 596
Puerperium, lung water during (MacLennan, MacDonald & Campbell), 141
Pulmonary artery catheterisation, benefits of (Wilkins & Edwards: Stoddart), 436 (c)
Pulmonary oedema, phaeochromocytoma as a cause of (Blom *et al.*), 646
Pulmonary oedema, unilateral, in the lateral decubitus position (Baraka, Moghrabi & Yazigi), 171
Pulmonary nitrogen washout, the effect of pregnancy; a study of pre-oxygenation (Byrne, Oduro-Dominah & Kipling), 148
Pulse oximeter—an early warning device? (Mason), 784 (c)
Pulse oximeter, erroneous activation (Norley: Taylor), 1116 (c)
Pumps, Graseby PCAS, a potential hazard (Hanning, Ogden & Parry: Coombs), 559 (c)
Pupil, action of narcotics on (Larson), 566 (c)
Pupils, dilated, fixed, following cardiac surgery (Carter & Weston), 1231 (c)
Pyrexia associated with a retroperitoneal tumour (Eddleston), 213 (c)

Radial artery, abscess following cannulation of (Lindsay, Kerridge & Collett), 654
Radial artery cannulation, local tissue oxygenation after (Murray & Mowbray), 1070
Rapid inhalation induction (Galloway: Wilton & Thomas), 772 (c)
Recovery period, nerve palsy occurring during (Hughes-Davies), 326 (c)
Recovery from propofol infusion as the main agent for outpatient arthroscopy; a comparison with isoflurane (Zuurmond, van Leeuwen & Helmers), 356
Recovery times (Cundy), 89 (c)
Recurarisation after vecuronium in a patient with renal failure (Cody & Dormon), 993
Red patient: immunological reaction to glycine? (Moskovits, Riches & Soni), 962
Regional techniques, two, compared for postoperative analgesia in children following herniotomy and orchidopexy (Cross & Barrett), 845
Regulator, gas-loaded, defective, awareness under anaesthesia due to (Puti *et al.*), 539
Relaxant and nitrous oxide anaesthesia, comparison of trichloroethylene and enflurane as adjuncts to (Rice & Reynolds), 1320 (f)
Renal dysfunction, prolonged paralysis following an infusion of alcuronium in a patient with (Smith, Hunter & Jones), 522
Renal failure and pancuronium (Sangala & Dixon: Hunter), 1236 (c)
Renal failure, recurisation after vecuronium in a patient with (Cody & Dormon), 993
Renal failure, vecuronium infusions in patients with, in an ITU (Smith, Hunter & Jones), 387
Renal impairment prevention, by infusion of low dose dopamine, in patients undergoing orthotopic liver grafting (Polson *et al.*), 15
Reservoir volume in a drawover system (Yoganathan, Johnston & Houghton: Mackie), 1337 (c)
Resistance to cardioplegia (Miller & Dougall), 1117 (c)
Resistance, suxamethonium, and hypercholinesterasaemia (Warran *et al.*), 855
Respiratory arrest after epidural sufentanil (Blackburn), 665 (c)
Respiratory arrest, delayed, after epidural hydromorphone (Wüst & Bromage), 404
Respiratory depressant effects of nalbuphine and papaveretum as intramuscular premedication (Rutter, Aveling & Tusiewicz), 1176
Respiratory depression in children at different end tidal halothane concentrations (Lindahl, Yates & Hatch), 1267
Respiratory depression after intrathecal opioids; long-term epidural opioid therapy (Krantz & Christensen), 168
Respiratory depression, morphine-induced, in the elderly (Bourke: Bowen *et al.*), 428 (c)
Respiratory depression, neonatal, clinically significant, absence of, after prolonged maternal propofol administration (Bloor, Jones & Turner), 1233 (c)
Respiratory depression, prolonged, buprenorphine and benzodiazepines (Sekar & Mimpriss), 567 (c)
Respiratory depression, prolonged and biphasic, following epidural buprenorphine (Jensen *et al.*), 470
Respiratory effects of isoflurane, enflurane and halothane in spontaneously breathing children (Murat *et al.*), 711
Respiratory function, in one lung anaesthesia, during conventional ventilation and high frequency jet ventilation (Jenkins *et al.*), 938

Respiratory obstruction following vocal cord injection, a complication on induction of anaesthesia (Bodenham, Latimer & Bethune), 289
Response rates (Chater & Simpson), 328 (c)
Resuscitation, cardiopulmonary, in district general hospitals (Newman), 314 (c)
Retention of auditory information presented during anaesthesia; study of children who received light general anaesthesia (Standen, Hain & Hosker), 604
Retirement, early, and morbidity (Adams: Hutchinson: Keen & McNamee), 1024 (c)
Retirement, early, and morbidity among anaesthetists and other specialists (McNamee, Keen & Corkill), 133
Retrobulbar block, attempted, prolonged haemodynamic disturbance following (Cardan, Pop & Negrutiu), 668 (c)
Retrobulbar spontaneous haemorrhage following anaesthesia (Gunning & Collett), 875
Retrograde intubation; management of a 4.8-kg, 5-month infant (Cooper & Murray-Wilson), 1197
Retroperitoneal tumour, pyrexia associated with (Eddleston), 213 (c)
Rotameter valves, open, potential leaks through (McQuillan & Jackson), 1308
Royal College of Surgeons of England, Faculty of Anaesthetists, 110
Royal College of Surgeons in Ireland, Faculty of Anaesthetists, 111
Royal Society of Medicine, Section of Anaesthetics, 111

Safety Information Bulletins, 129, 797, 1254
Safety of a new system for continuous airway pressure (Clayton & Catling), 440 (c)
Safety, protocol for (Kalla), 667 (c)
Sampling for carbon dioxide (Allen & Wren), 560 (c)
Scavenging, is it working? (Railton, Milton & Davie), 86 (c)
Scavenging systems, passive or active? (Kipling & Bethune), 777 (c)
Sciatic nerve block, use of a low-power nerve stimulator during (Smith & Allison), 296
Sedation in intensive care, propofol infusion for (Newman *et al.*), 929
Sedation, intravenous, for cataract surgery (Gilbert *et al.*), 1063
Sedation, intravenous, propofol for (Mackenzie & Grant), 3
Sedative, ketamine infusion used as, in a critically ill patient (Park *et al.*), 980
Sedation, long-term, in intensive care; assessment of alfentanil by intravenous infusion (Cohen & Kelly), 545 (f)
Selectatec vaporizer, broken control on (Davies: Smith), 215 (c)
Septo-optic dysplasia and anaesthesia; implications of missed diagnosis in the peri-operative period (Sherlock & McNicol), 1302
Serological markers for hepatitis B (Newcombe), 1239 (c)
Serological markers for hepatitis B virus infection, prevalence amongst anaesthetists in the Oxford region (Sinclair, Ashby & Kurtz), 30
Serum fluoride levels in morbidly obese patients; enflurane compared with isoflurane anaesthesia (Strube, Hulands & Halsey), 685
Serum myoglobin, effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on (Laurence), 503
Servo 900C ventilator, computer study; peak intratracheal pressure during controlled ventilation in infants and children (Synnott, Wren & Davenport), 719
Shelf-life of sodium citrate (0.3M) (Burgess & Wrobel), 1019 (c)
SI units, Newtons and apples (Rye), 1025 (c)
Side effects after a single dose of epidural fentanyl or sufentanil during elective Caesarean section (Madej & Strunin), 1156
Silencers for jet ventilators, hazard of (Van Besouw), 81 (c)
Sinus arrest; non vagolytic anaesthetic sequence (Thorp & Higgins), 432 (c)
Skin damage and primary amyloidosis (Dixon), 218 (c)
Smoking and anaesthesia: editorial (Jones, Rosen & Seymour), 1
Smoking and anaesthesia (Symons), 569 (c)
Smoking and anaesthesia (Callander: McKechnie: Jones & Rosen), 770 (c)
Sodium citrate (0.3M), shelf-life of (Burgess & Wrobel), 1019 (c)
Somatostatin, anaesthesia, and the carcinoid syndrome; peri-operative administration of a somatostatin analogue to suppress carcinoid tumour activity (Roy, Carter & Wright), 627
Sore throat, postoperative; comparison of Magill and Mallinckrodt tracheal tubes (Sprague & Archer), 306 (f)
Sore throat, postoperative, interview method affects incidence of (Harding & McVey), 1104 (f)
Spasm of the sphincter of Oddi can be avoided (Vatashsky & Haskel), 564 (c)
Speech synthesiser, feedback during patient-controlled analgesia using (Hodsman *et al.*), 767 (f)
Sphincter of Oddi, spasm can be avoided (Vatashsky & Haskel), 564 (c)
Spinal anaesthesia, bradycardia and hypotension in (Hutter), 89 (c)
Spinal anaesthesia for Caesarean section (Hollis, White & Procter), 323 (c)
Spinal anaesthesia for Caesarean section (Kirkwood), 900 (c)
Spinal anaesthesia following facet joint injection, report of two cases (Goldstone & Pennant), 754
Spinal anaesthesia, postoperative headache in young patients after (Flaatten *et al.*), 202 (f)
Spinal anaesthesia in pregnant patients (Edmondson & Erwin), 666 (c)

Spinal anaesthesia, transient hearing loss following (Wang, Fog & Bove), 1258
Spinal cord compression during chronic epidural morphine administration in a cancer patient (van Diejen, Driessen & Kaanders), 1201
Splenectomy and splenorenal shunt formation in a patient with systemic mastocytosis; histamine levels and cardiovascular responses during (Smith *et al.*), 861
Spring guide wire, transvenous misplacement and loop formation of (Kjeldsen), 216 (c)
ST segment analysis, computerised, in comparison of different lead systems; myocardial ischaemia during non-cardiac surgery (Griffin & Kaplan), 155
Standards, international, deviations from (Shankar), 444 (c)
Stents, bronchial, use in the management of bronchomalacia (Goddard & Booker), 534
Stents, intratracheal, insertion of; anaesthetic management using high frequency jet ventilaton or cardiopulmonary bypass (Sherry *et al.*), 61
Stethoscope, oesophageal (O'Dea & Hall), 1337 (c)
Subarachnoid block with hyperbaric lignocaine; comparison with hyperbaric bupivacaine (Ewart & Rubin), 1183
Subclavian steal syndrome and anaesthesia (Read), 442 (c)
Subdural catheterisation, accidental (Treffers & de Lange: Lee & Dodd), 556 (c)
Subtrigonal phenol, cardiac dysrhythmia after (Forrest & Ramage), 777 (c)
Suction, tracheal, difficult (Prince, Perks & Fraser), 84 (c)
Sufentanil, effect on the cardiovascular responses to tracheal intubation (Kay *et al.*), 382
Sufentanil, epidural, large dose; management of postoperative pain with few side effects (Madej, Watson & Martin), 1204
Sufentanil, epidural, respiratory arrest after (Blackburn), 665 (c)
Sufentanil, epidural, versus intramuscular buprenorphine for postoperative analgesia (Donadoni & Rolly), 1171
Sufentanil and fentanyl, epidural, a comparison; analgesia and side effects after a single bolus dose during elective Caesarean section (Madej & Strunin), 1156
Sufentanil low dose pretreatment, effect on induction of anaesthesia with thiopentone, methohexitone or midazolam (Furness, Dundee & Milligan), 1264
Suggestion, intra-operative, and operating room conversation, pyschological sequelae in cardiac patients; memory of cardiac anaesthesia (Goldmann, Shah & Hebden), 596
Supine faints (Paul & McKeown), 1120 (c)
Suppuration, epidural, extensive, epidural lavage for (Cardan & Nanulescu), 1023 (c)
Supraclavicular brachial plexus block, unilateral thoraco-abdominal blockade following (Manara), 757
Surgery, abdominal; the morphine sparing effect of ketorolac tromethamine (Gillies *et al.*), 727
Surgery, abdominal, the morphine sparing effects of diclofenac sodium following (Hodsman *et al.*), 1005 (f)
Surgery, aortic aneurysm, intrathecal morphine in (Davis), 491
Surgery, aortocoronary bypass graft; comparison of conventional intermittent positive pressure ventilation with high frequency jet ventilation (Normandale *et al.*), 824
Surgery, carbon dioxide laser, in tracheobronchial lesions; anaesthetic management (Hunton & Oswal), 1222 (f)
Surgery, cardiac, acute effects of intravenous isosorbide dinitrate during (Parsons, Wetzel & Mohandas), 498
Surgery, cardiac, continuous display of plasma potassium during (Drake, Treasure & Smith), 23
Surgery, cardiac, fixed dilated pupils following (Carter & Weston), 1231 (c)
Surgery, carotid artery, cervical epidural analgesia during (Campkin: Kainuma & Shimada), 437 (c)
Surgery, cataract, intravenous sedation for (Gilbert *et al.*), 1063
Surgery, concurrent drug therapy in patients undergoing (Duthie *et al.*), 305 (f)
Surgery, coronary artery bypass, in a patient with suspected malignant hyperpyrexia, propofol infusion for (Richardson), 1125 (c)
Surgery, day case; a study of oral midazolam for premedication (Raybould & Bradshaw), 591
Surgery, elective, blood tests before (Jacobsen, Bach & Dalsgaard), 78 (c)
Surgery, eye, emergency, control of intra-ocular pressure during the induction of anaesthesia; a high dose vecuronium technique (Abbott & Samuel), 1008 (f)
Surgery, eye, prochlorperazine and vomiting after (van den Berg & Lambourne), 898 (c)
Surgery, hip, nerve blocks for (Rice & Pither: Smith & Allison), 1016 (c)
Surgery, the influence of anaesthesia on the acute phase protein response to (Simpson, Radford & Lockyer), 690
Surgery, intra-abdominal, bradycardia during; modification by pre-operative anticholinergic agents (Coventry, McMenemin & Lawrie), 835
Surgery, microlaryngeal, comparison of etomidate and propofol anaesthesia (de Grood *et al.*), 366
Surgery, middle ear, hypotensive anaesthesia for (Williamson: Eltringham & Fairbairn), 669 (c)
Surgery, non-cardiac, myocardial ischaemia during; a comparison of different lead systems using computerised ST segment probes (Griffin & Kaplan), 155
Surgery, ophthalmic, vomiting after; effects of intra-operative antiemetics and postoperative oral fluid restriction (van de Berg *et al.*), 270
Surgery, oral, influence of premedication on the occurrence of dysrhythmias during (Smith & O'Connell), 882 (f)
Surgery, phaeochromocytoma, hypoglycaemic encephalopathy following (Channa *et al.*), 1298

Surgery, steady-state neuromuscular blockade during, using a computer controlled closed-loop atracurium infusion (Webster & Cohen), 1085
Surgery, valvular heart; comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation (Sherry, Windsor & Feneck), 1276
Surgical packs, antiseptic, gross hypernatraemia associated with the use of (Thorp, Mackenzie & Simpson), 750
Surgical packs, antiseptic, gross hypernatraemia associated with the use of (Wise: Thorp, MacKenzie & Simpson), 1331 (c)
Suxamethonium administration, intermittent, myalgia and biochemical changes following; effects of alcuronium, lignocaine, midazolam and suxamethonium pretreatments on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Suxamethonium, a study in allergy to; basophil histamine release (Withington *et al.*), 850
Suxamethonium apnoea in a 4-month-old twin (Mehta & Hole), 868
Suxamethonium, beta blockade and potassium (Goldhill & Martyn), 670 (c)
Suxamethonium in myasthenia gravis (Wainwright & Brodrick), 950
Suxamethonium pretreatment, effect on serum myoglobin, creatine kinase and myalgia (Laurence), 503
Suxamethonium resistance and hypercholinesterasaemia (Warren *et al.*), 855
Suxamethonium-induced rise in plasma potassium, and beta-adrenoceptor blockade (Maryniak *et al.*), 71 (f)
Sympathetic blockade, upper limb, following intercostal nerve blocks (Purcell-Jones, Speedy & Justins), 984
Systemic mastocytosis, histamine levels and cardiovascular responses during splenectomy and splenorenal shunt formation in a patient with (Smith *et al.*), 861

Table knife transducer; monitoring neuromuscular blockade (Dundas, Levack & Brockway), 1092
Tactile orotracheal tube placement test; bimanual tactile examination of the positioned orotracheal tube to confirm laryngeal placement (Charters & Wilkinson), 801
Test doses, epidural, obstetric (Cartwright), 556 (c)
Textbooks, early, on anaesthesia (Secher), 1022 (c)
Thiopentone anaesthesia, effect of low dose sufentanil pretreatment (Furness, Dundee & Milligan), 1264
Thiopentone anaesthesia for laparoscopy, comparison with propofol, etomidate and isoflurane (de Grood *et al.*), 815
Thiopentone anaesthetic properties, comparison with pregnanolone emulsion (Høgskilde *et al.*), 1045
Thiopentone and propofol, relative potency (Grant & Mackenzie: O'Connor & Wilkinson: Grounds, Taylor & Morgan), 317 (c)
Thiopentone and propofol, relative potency (Kay), 1025 (c)
Thoraco-abdominal unilateral blockade following the supraclavicular approach; brachial plexus block (Manara), 757
Tourniquet, pneumatic, paralysis following intravenous regional analgesia (Larsen & Hommelgaard), 526
T-piece, Ayre's, an antipollution device for use with the Jackson–Rees modification of (Paul), 439 (c)
T-piece, Ayre's, improved antipollution device for the Jackson–Rees modification of (Spargo, Apadoo & Wilton), 1240 (c)
Trachea, transnasal anaesthesia of (Kartha & Cyriac-Mathew), 320 (c)
Tracheal versus intravenous atropine; comparison of the effects on heart rate (Bray, Jones & Grundy), 1188
Tracheal intubation, attempted, piriform fossa perforation during (Wengen), 519
Tracheal intubation in beta-blocker treated hypertensive patients, intranasal nitroglycerine attenuates pressor response to (Grover *et al.*), 884 (f)
Tracheal intubation, difficult (Sellers & Yogendran), 1243 (c)
Tracheal intubation, difficult, cellulitis as a complication of (Young & Robinson), 569 (c)
Tracheal intubation, difficult, modified Magill forceps for (Pelimon & Simunovic), 83 (c)
Tracheal intubation, difficult, modified Magill forceps for (Vonwiller, Liberman & Maver), 777 (c)
Tracheal intubation, difficult, a retrospective study (Samsoon & Young), 487
Tracheal intubation, difficult, due to tracheopathia osteochondroplastica (Smith, Pillai & Gillbe), 536
Tracheal intubation, failed, propofol in (Coleman & Phillips), 1233 (c)
Tracheal intubation, the effect of sufentanil on the cardiovascular responses to (Kay *et al.*), 382
Tracheal suction, difficult (Prince, Perks & Fraser), 84 (c)
Tracheal tube, Argyll, a problem with (Scott & Chapman), 1123 (c)
Tracheal tubes, Magill versus Mallinckrodt; comparative study of postoperative sore throat (Sprague & Archer), 306 (f)
Tracheal tubes in neuroanaesthesia; nylon reinforced latex rubber tracheal tubes (Wright & Mundy), 1012 (f)
Tracheal tube, postmortem removal of (Watson: Knight & Addicott), 554 (c)
Tracheal tube, postmortem removal of (Johnston & Charters), 1242 (c)
Tracheal tubes, shaping (Kubota *et al.*), 896 (c)
Tracheobronchial lesions, anaesthetic management for carbon dioxide laser surgery in (Hunton & Oswal), 1222 (f)
Tracheopathia osteochondroplastica, a cause of unexpected difficulty in tracheal intubation (Smith, Pillai & Gillbe), 536
Training in fibreoptic techniques (Mostafa), 429 (c)
Transducer, Grass FT03, limitations of (Sosis: Jones), 85 (c)

Transducer, table knife; monitoring neuromuscular blockade (Dundas, Levack & Brockway), 1092
Transillumination in fibreoptic intubation (Whitlock & Calder), 570 (c)
Transnasal anaesthesia of the pharynx, larynx and trachea (Kartha & Cyriac-Mathew), 320 (c)
Transport, oximetry during (Finfer & Wishaw), 900 (c)
Transportation, postoperative, arterial oxygen desaturation during; the influence of operation site (Meiklejohn *et al.*), 1313 (f)
Transvenous misplacement and loop formation of spring guide wire (Kjeldsen), 216 (c)
Triazolam premedication (Pinnock & Fell: Tipping, Blogg & Thomas), 316 (c)
Trichloroethylene and enflurane compared as adjuncts to nitrous oxide and relaxant anaesthesia (Rice & Reynolds), 1320 (f)
Trichloroethylene and halothane compared with isoflurane; a study of drawover air anaesthesia with the Triservice anaesthetic apparatus (Tighe & Pethybridge), 887 (f)
Triservice anaesthetic apparatus, drawover air anaesthesia with; halothane and trichloroethylene compared with isoflurane (Tighe & Pethybridge), 887 (f)
Triservice anaesthetic apparatus; trial of isoflurane and enflurane as alternatives to halothane (Kocan), 1101 (f)
Tubal ligation, arterial to end tidal carbon dioxide tension difference during anaesthesia for (Shankar *et al.*), 482
Tubal ligation, arterial to end tidal carbon dioxide tension difference during anaesthesia for (Puri: Shankar *et al.*), 1338 (c)
Tube, coaxial, inner, unattached (Roberts), 1128 (c)
Tube, down the: editorial (Greenbaum), 927
Tube, kinked, or bronchospasm? (Ross), 441 (c)
Tube, pilot, kinked (Tanski & James), 1022 (c)
Tube, pilot, kinked, difficult extubation due to (Mehta), 443 (c)
Tubes, *see also* Tracheal tubes
Tumour, cerebral, epidural anaesthesia in the presence of (Chater, Greig & Sugden: Kinsella: Francis: Goroszeniuk & Wright), 433 (c)
Tumours, liver, and muscle relaxants; electromyographic studies in children (Brown *et al.*), 1284
Tumour, retroperitoneal, pyrexia associated with (Eddleston), 213 (c)
Twin deliveries, consecutive, 200, a prospective study of (Crawford), 33
Twin, 4-month-old, suxamethonium apnoea in (Mehta & Hole), 868

Unilateral pulmonary oedema/atelectasis in the lateral decubitus position (Baraka, Moghrabi & Yazigi), 171
Unit of applied force (Wilson), 86 (c)
Units, Newtons and apples (Rye), 1025 (c)
Upper airway obstruction during anaesthesia, asymptomatic epiglottic cysts as a cause of (Mason & Wark), 407
Upper airway obstruction in neurofibromatosis (Crozier), 1209
Upper airways obstruction, an unusual cause of (Aldridge), 1239 (c)
Upper limb sympathetic blockade following intercostal nerve blocks (Purcell-Jones, Speedy & Justins), 984

Vagal activity, afferent, and high frequency ventilation (Harrop-Griffiths, Chakrabarti & Whitwam), 1162
Valves; drilled for safety (Nott), 563 (c)
Valves, Rotameter, open, potential leaks through (McQuillan & Jackson), 1308
Valvular heart surgery; comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation (Sherry, Windsor & Feneck), 1276
Vaporizers, free-standing, a hazard (Van Besouw & Thurlow), 671 (c)
Vaporizer mounting, off-line, Penlon, another hazard with (Woollam), 781 (c)
Vaporizer, Selectatec, broken control on (Davies: Smith), 215 (c)
Vecuronium, bradycardia associated with the use of; comparison with pancuronium, with and without glycopyrronium (Cozanitis, Pouttu & Rosenberg), 192 (f)
Vecuronium, effects on intra-ocular pressure (Mirakhur *et al.*), 944
Vecuronium infusions in patients with renal failure in an ITU (Smith, Hunter & Jones), 387
Vecuronium in obstetrics, priming with (Cherala *et al.*), 1021 (c)
Vecuronium after pancuronium; economy in the use of muscle relaxants (Kay *et al.*), 277
Vecuronium, prolongation of neuromuscular blocking effect of, by antibiotics (Jedeikin *et al.*), 858
Vecuronium, recurarisation after, in a patient with renal failure (Cody & Dormon), 993
Vecuronium—a variable dose technique (Feldman & Liban), 199 (f)
Venous, central catheter, pleural aspiration with (Cooper), 217 (c)
Venous, central catheter, pleural aspiration with (Thorp), 896 (c)
Venous pressure, central, spurious (Barrowcliffe), 293
Ventilation, artificial, bowel sounds during (Manara, Kinnear & Park), 668 (c)
Ventilation, combined unilateral high frequency jet and contralateral intermittent positive pressure (Morgan *et al.*), 975
Ventilation, controlled, in infants, intratracheal pressure during (Drummond: Synnott, Wren & Davenport), 1332 (c)

Ventilation, controlled, in infants and children, peak intratracheal pressure during; computer study of the Servo 900C ventilator (Synnott, Wren & Davenport), 719
Ventilation, conventional intermittent positive pressure, compared with the high frequency jet ventilation; studies following aortocoronary bypass graft surgery (Normandale *et al.*), 824
Ventilation, conventional and high frequency jet, comparison of cardiovascular and respiratory function during, for one lung anaesthesia (Jenkins *et al.*), 938
Ventilation, high frequency, and afferent vagal activity (Harrop-Griffiths, Chakrabarti & Whitwam), 1162
Ventilation, high frequency jet, and arterial to end tidal carbon dioxide difference (Shankar), 1124 (c)
Ventilation, high frequency jet, for bilateral bullectomy (McCarthy *et al.*), 411
Ventilation, high frequency jet, compared with intermittent positive pressure ventilation; studies following aortocoronary bypass graft surgery (Normandale *et al.*), 824
Ventilation, high frequency jet, displacement of a minitracheotomy tube during (Ravalia & Stockwell), 1306
Ventilation, high frequency jet; insertion of intratracheal stents (Sherry *et al.*), 61
Ventilation, intermittent positive pressure, bowel sounds during (Shelly & Church), 207 (c)
Ventilation, long-term, contamination control in; a clinical study using a heat- and moisture-exchanging filter (Gallagher, Strangeways & Allt-Graham), 476
Ventilator, new, for closed breathing systems (Twigley, Chakrabarti & Whitwam), 419
Ventilator, new, for closed breathing systems (James: Plenderleith: Twigley, Chakrabarti & Whitwam), 1335 (c)
Ventilator, Nuffield 200, another modification of (Kwan & See: Calhaem), 80 (c)
Ventilation and the oculocardiac reflex (Blanc: Mirakhur & Jones), 324 (c)
Ventilation, spontaneous, in old people (Keen), 568 (c)
Ventilator alarms, should they be compulsory? (Gilston), 667 (c)
Ventilators, jet, hazard of silencers for (Van Besouw), 81 (c)
Ventolin nebules (Mackie), 1332 (c)
Vigilance, a matter of (James: McDowell: Green), 313 (c)
Vigilance, a matter of (Allen *et al.*: Green), 434 (c)
Vigilance, minimal monitoring and: editorial (Mathias & Lunn), 683
Vocal cord injection, respiratory obstruction following; a complication on induction of anaesthesia (Bodenham, Latimer & Bethune), 289
Volatile anaesthetics, use in the New World (Strunin & Davies), 774 (c)
Vomiting after eye surgery, and prochlorperazine (van den Berg & Lambourne), 898 (c)
Vomiting following ophthalmic anaesthesia (van den Berg: Mostafa & Lockhaert), 897 (c)
Vomiting after ophthalmic surgery; effects of intra-operative antiemetics and postoperative oral fluid restriction (van den Berg *et al.*), 270
Vomiting after prostaglandins in day case termination of pregnancy; the efficacy of low dose droperidol (Millar & Hall), 613

Wales, use of protocols in obstetric units in 1983 (Owen), 1323 (f)
Water bath blood warmers, risk of infection from (Bray), 778 (c)
Wedge, paediatric, inflatable (Bembridge), 213 (c)
Wire, guide, in assistance of arterial cannulation; a complication (McMenemin & Kenny: McGregor), 562 (c)
Wire, spring guide, transvenous misplacement and loop formation of (Kjeldsen), 216 (c)
Wound infiltration compared with ilio-inguinal nerve block for postoperative analgesia; day case herniotomy in children (Reid *et al.*), 658 (f)

Young patients, postoperative headache after spinal anaesthesia (Flaatten *et al.*), 202 (f)

Zidovudine and the anaesthetist: editorial (Phillips & Spence), 799
Zygomatic fractures, bradycardia during elevation of; a variation of the oculocardiac reflex (Shearer & Wenstone), 1207

Key Word Index, Volume 42 (1987)

Allergy, 164, 1078
Anaesthesia, inhalational, 299
Anaesthesia, intravenous, 1218
Anaesthesia, obstetric, 148, 160, 346, 352, 482, 745, 877, 1323
Anaesthesia, outpatient, 373, 658
Anaesthesia, paediatric, 541, 711, 719, 879, 1197, 1267, 1316
Anaesthesia, paediatric, outpatient, 658
Anaesthesia, paediatric, prune-belly syndrome, 54
Anaesthesia, spinal injury, 877
Anaesthesia, thoracic, 536, 938

Anaesthesia, urological, 171
Anaesthetic gases, nitrous oxide, 609
Anaesthetic techniques, acupuncture, 1108
Anaesthetic techniques, epidural, 33, 160, 168, 377, 404, 470, 643, 1098, 1110, 1171, 1180, 1201, 1204, 1258
Anaesthetic techniques, heart–lung transplantation, 249
Anaesthetic techniques, induced hypotension, 243
Anaesthetic techniques, infusion, 387, 1085
Anaesthetic techniques, inhalational, 887
Anaesthetic techniques, intrathecal narcotics, 491
Anaesthetic techniques, local, lignocaine, 1183
Anaesthetic techniques, pre-oxygenation, 1008
Anaesthetic techniques, rapid sequence induction, 944
Anaesthetic techniques, regional, brachial plexus, 757
Anaesthetic techniques, regional, caudal, 845
Anaesthetic techniques, regional, epidural, 33, 160, 168, 377, 404, 643, 1098, 1110, 1171, 1201, 1204
Anaesthetic techniques, regional, facet joint blockade, 754
Anaesthetic techniques, regional, iliohypogastric and ilio-inguinal block, 845
Anaesthetic techniques, regional, ilio-inguinal block, local infiltration, 658
Anaesthetic techniques, regional, intercostal block, 541, 958, 984
Anaesthetic techniques, regional, intravenous, 1078, 1081
Anaesthetic techniques, regional, local infiltration, 658
Anaesthetic techniques, regional, sciatic nerve block, 296
Anaesthetic techniques, regional, spinal, 3, 168, 202, 1183, 1258
Anaesthetic techniques, tracheal intubation, 884
Anaesthetics, intravenous, Althesin, 586, 1045
Anaesthetics, intravenous, droperidol, 613
Anaesthetics, intravenous, etomidate, 366, 815
Anaesthetics, intravenous, ketamine, 411, 980, 1051
Anaesthetics, intravenous, methohexitone, 373, 1264
Anaesthetics, intravenous, pregnanolone, 586, 1045
Anaesthetics, intravenous, propofol, 3, 356, 360, 366, 373, 815, 929, 1045
Anaesthetics, intravenous, thiopentone, 815, 1045, 1264
Anaesthetics, local, bupivacaine, 377, 1183
Anaesthetics, volatile, enflurane, 711, 1191, 1320
Anaesthetics, volatile, halothane, 189, 259, 690, 711, 887, 1267
Anaesthetics, volatile, isoflurane, 189, 259, 356, 711, 815, 887
Anaesthetics, volatile, trichloroethylene, 887, 1320
Analgesia, obstetric, 33, 661, 697, 1098
Analgesia, opioids, 1316
Analgesia, postoperative, 727
Analgesics, intravenous, fentanyl, 195
Analgesics, narcotic, alfentanil, 545, 1218
Analgesics, narcotic, buprenorphine, 470, 1171
Analgesics, narcotic, fentanyl, 690, 1063, 1156, 1204, 1218
Analgesics, narcotic, hydromorphone, 404
Analgesics, narcotic, meptazinol, 7
Analgesics, narcotic, morphine, 704, 1005, 1051
Analgesics, narcotic, morphine, sustained release morphine, 840
Analgesics, narcotic, nalbuphine, 697, 704, 1063, 1176
Analgesics, narcotic, papaveretum, 1176
Analgesics, narcotic, pethidine, 7, 697
Analgesics, narcotic, sufentanil, 383, 1156, 1171, 1204, 1264
Analgesics, non-narcotic, diclofenac, 1005
Analgesics, non-narcotic, indomethacin, 202
Analgesics, non-steroidal, 727
Anatomy, airway, 1209
Antibiotics, clindamycin, 858
Antibiotics, gentamycin, 858
Ataractics, phenothiazines, 49

Blood, 639
Blood, anticoagulant, 1291
Blood, coagulation, 1291
Blood, loss, 44
Brain, evoked potentials, 195

Co-existing disease, De Morsier's syndrome, 1302
Co-existing disease, malignant disease, 1284
Co-existing disease, septo-optic dysplasia, 1302
Co-existing disease, systemic mastocytosis, 861
Complications, 757, 1110
Complications, accident, 1012
Complications, acute renal failure, 15
Complications, anaphylaxis, 850, 998
Complications, asthma, 1287
Complications, atelectasis, pulmonary oedema, 171
Complications, awareness, 539, 596, 604
Complications, bradycardia, 192, 1207, 1294
Complications, carcinoid tumour, 627
Complications, cardiac arrest, 1074
Complications, cardiac dysrhythmias, 189
Complications, coma, 1302
Complications, convulsions, 1302
Complications, death, 643
Complications, displacement of minitracheotomy tube, 1306
Complications, dural puncture, 1180
Complications, dysrhythmia, 882
Complications, dystrophia myotonica, 529
Complications, fracture, cervical spine, 745
Complications, headache, 202
Complications, hearing loss, 1258
Complications, hepatitis B virus infection, 30
Complications, histamine release, 861
Complications, hyperkalaemia, 71
Complications, hypertension, 633
Complications, hyperthermia, 49
Complications, hypoglycaemic encephalopathy, 1298
Complications, hypotension, 754, 1081, 1294
Complications, infection, 1201
Complications, intubation, nasotracheal, 651
Complications, intubation, tracheal, 382, 407, 519, 536
Complications, muscle relaxant resistance, 1284
Complications, myalgia, 503
Complications, myasthenia gravis, 950
Complications, myocardial ischaemia, 155
Complications, myoglobinaemia, 503
Complications, nausea, 1108
Complications, nerve damage, 526, 654
Complications, obesity, 685
Complications, pneumonia, 54
Complications, postoperative, 1320
Complications, postoperative sore throat, 306
Complications, prolonged apnoea, 868
Complications, prolonged neuromuscular blockade, 858
Complications, pulmonary oedema, 646
Complications, raised intra-ocular pressure, 259
Complications, recurarisation, 993
Complications, respiratory depression, 168
Complications, respiratory obstruction, 289
Complications, retrobulbar haemorrhage, 875
Complications, sore throat, 306, 1104
Complications, systemic lupus erythematosus, 1291
Complications, uraemia, 54
Complications, vomiting, 1108

Drug interactions, 760, 1294
Drugs, pre-operative treatment, 305

Enzymes, 855, 868
Equipment, 767
Equipment, anaesthetic machines, 1308

Equipment, bacterial filter, 476
Equipment, breathing systems, minimum fresh gas flows, 732
Equipment, bronchoscopes, 996
Equipment, catheters, arterial, 1070
Equipment, catheters, epidural, 182, 661
Equipment, catheters, venous, 67
Equipment, drawover, 299
Equipment, electromyographs, 1212
Equipment, fail-safe, 539
Equipment, heat and moisture exchanger, 476
Equipment, infusion pumps, 1212
Equipment, ion-selective electrodes, 23
Equipment, laryngoscope, 764, 877
Equipment, lasers, 511
Equipment, nerve stimulators, 1212
Equipment, oxygen analysers, 175
Equipment, Rotameters, 1308
Equipment, tourniquets, 526
Equipment, tracheal tubes, 306, 1012
Equipment, Triservice anaesthetic apparatus, 1101
Equipment, ventilators, 419, 476
Explosions, 186

Gases, non-anaesthetic, air, 609
Gastrointestinal tract, 704
Genetic factors, glucose-6-phosphate dehydrogenase deficiency, 281

Heart, 636
Heart, bradycardia, 835
Histamine, 850
History, Brünings, Wilhelm, 996
History, Magill, 1096
Hormones, 627
Hyperthermia, 760
Hypnotics, benzodiazepines, diazepam, 808, 1063
Hypnotics, benzodiazepines, lormetazepam, 808
Hypnotics, benzodiazepines, midazolam, 591, 619, 1045, 1057, 1264
Hypnotics, methohexitone, 1063
Hypothermia, 415
Hypoxia, postoperative, 1313

Immune response, 962
Inotropes, 15
Intensive care, 415, 476, 545, 738, 929, 980
Interactions, drug, 760, 1294
Ions, 23, 750
Intravenous infusion, gelatin solutions, 998
Intubation, orotracheal, 801
Intubation, tracheal, 764, 877, 1096
Intubation, tracheal, difficult, 487, 1209
Intubation, tracheal, technique, 1197
Intubation, tracheal, *see also* Complications

Jehovah's Witness, 44

Kidney, failure, 993

Larynx, epiglottic cyst, 407
Larynx, reflexes, 808
Liver, toxicity, 1191
Lung, bronchus, 534
Lung, trachea, 1188
Lung, water, 141

Manpower, anaesthetists, 133
Measurement techniques, audiometry, 1258
Measurement techniques, capnography, 482, 1156
Measurement techniques, carbon dioxide response, 1176

Measurement techniques, intra-ocular pressure, 266
Measurement techniques, neuromuscular blockade, 1092
Measurement techniques, oximetry, 879, 1313
Measurement techniques, radio-immunoassay, 1156
Measurement techniques, vagus nerve activity, 1162
Measurement techniques, visual analogue scale, 1156
Memory, 596
Metabolism, anaesthetics, 685
Monitoring, blood pressure, 654
Monitoring, electrocardiogram, 155

Neuromuscular blockade, 1092
Neuromuscular relaxants, alcuronium, 164
Neuromuscular relaxants, alcuronium, prolonged action, 522
Neuromuscular relaxants, atracurium, 259, 1085, 1212
Neuromuscular relaxants, pancuronium, 192, 277
Neuromuscular relaxants, suxamethonium, 71, 503, 855, 950
Neuromuscular relaxants, vecuronium, 192, 199, 277, 387, 944, 1008

Oxygen, breathing systems, 346
Oxygen, delivery systems, 148

Pain, 7, 767, 840, 845
Parasympathetic nervous system, atropine, 1188
Pharmacokinetics, 619, 1057
Pharmacology, 352, 633, 884, 989
Pharmacology, fluorocarbons, 234
Pharmacology, isosorbide dinitrate, 498
Pneumothorax, 987
Pregnancy, 141, 1074
Premedication, 591, 882
Premedication, atropine, 835
Premedication, glycopyrronium, 835
Protein, 690

Receptors, 394
Regional techniques, brachial plexus block, 20

Sterilisation, wounds, 750
Surgery, bronchoscopy, 511
Surgery, carcinoid tumour, 989
Surgery, cardiac, 498
Surgery, cardiac, transplantation, 249
Surgery, cardiovascular, 491
Surgery, faciomaxillary, 1207
Surgery, laser, 1222
Surgery, liver transplantation, 15
Surgery, microlaryngeal, 366
Surgery, ophthalmic, 266, 270
Surgery, ovarian cystectomy, 965
Surgery, phaeochromocytoma removal, 646, 1298
Surgery, tracheal, 61, 289
Surgery, tracheal, laser, 1222
Sympathetic nervous system, beta-adrenergic antagonists, 243

Technique, cardiopulmonary bypass, 61

Veins, cannulation, 151
Veins, venous pressure, 293
Ventilation, airway pressure, 719
Ventilation, apnoea, carbon dioxide response, 394
Ventilation, continuous positive pressure, 987
Ventilation, high frequency jet, 61, 411, 1162, 1276, 1306
Ventilation, high frequency jet, intermittent positive pressure, 824, 938, 975
Ventilation, intermittent positive pressure breathing, 1276
Ventilation, intermittent positive pressure, high frequency jet, 824, 938, 975
Ventilation, positive end expiratory pressure, 1276
Vomiting, 270, 613

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (UK).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × $10\frac{1}{2}$ in. or $8\frac{1}{2}$ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence are to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s), degrees and designations should be typed in lower case below the line. Initials should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.
(ii) Underlined words
These should be typed at the left-hand side of the page above the paragraph which they precede.
(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

Use the form of reference adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscripts submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the left-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS, ABBREVIATIONS AND STATISTICS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents, ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 42, no. 12, December 1987

EDITORIAL

Benzodiazepines
J.G. Whitwam 1255

ORIGINAL ARTICLES

Transient hearing loss following spinal anaesthesia
L.P. Wang, J. Fog and M. Bove 1258
Low dose sufentanil pretreatment. Effect on the induction of anaesthesia with thiopentone, methohexitone or midazolam
G. Furness, J.W. Dundee and K.R. Milligan 1264
Respiratory depression in children at different end tidal halothane concentrations
S.G.E. Lindahl, A.P. Yates and D.J. Hatch 1267
Comparison of the haemodynamic effects of intermittent positive pressure ventilation with high frequency jet ventilation. Studies following valvular heart surgery
K.M. Sherry, J.P.W. Windsor and R.O. Feneck 1276

CASE REPORTS

Liver tumours and muscle relaxants. Electromyographic studies in children
T.C.K. Brown, M. Gregory, B. Bell and P.C. Campbell 1284
Severe acute asthma and the menstrual cycle
R.J. Lenoir 1287
Lupus anticoagulant. Implications for obstetric anaesthetists
A.M. Malinow, W.J.K. Rickford, B.L.K. Mokriski, D.N. Saller and W.J. McGuinn 1291
Prolonged bradycardia and hypotension after neostigmine administration in a patient receiving atenolol
J. Eldor, B. Hoffman and J.T. Davidson 1294
Hypoglycaemic encephalopathy following surgery on phaeochromocytoma
A.B. Channa, A.B. Mófti, G.W. Taylor, M.O. Mekki and M.H. Sheikh 1298
Anaesthesia and septo-optic dysplasia. Implications of missed diagnosis in the peri-operative period
D.A. Sherlock and L.R. McNicol 1302
Displacement of a minitracheotomy tube during high frequency jet ventilation
A. Ravalia and M.A. Stockwell 1306

APPARATUS

Potential leaks from anaesthetic machines. Potential leaks through open Rotameter valves and empty cylinder yokes
P.J. McQuillan and I.J.B. Jackson 1308

FORUM

Arterial oxygen desaturation during postoperative transportation: the influence of operation site
B.H. Meiklejohn, G. Smith, A.E. Elling and N. Hindocha 1313
The use of opioids in neonates. A retrospective study of 933 cases
G. Purcell-Jones, F. Dormon and E. Sumner 1316
Comparison of trichloroethylene and enflurane as adjuncts to nitrous oxide and relaxant anaesthesia
A.S.C. Rice and F. Reynolds 1320
Protocols in obstetric units: their use in Wales in 1983
B. Owen 1323

CORRESPONDENCE 1327

ANAESTHETIC LITERATURE 1340

STOP PRESS 1350

INDEX 1351

Printed in Great Britain by Richard Clay Ltd, Bungay, Suffolk